

Substituted Pyrazolopyrimidines and Thiazolopyrimidines

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Cross-Reference to Related Applications

This application is a continuation of International Patent Application No. PCT/EP02/02722, filed March 13, 2002, designating the United States of America, and published in 10 German as WO 02/072585, the entire disclosure of which is incorporated herein by reference. Priority is claimed based on Federal Republic of Germany patent application no. DE 101 12 197.0, filed March 14, 2001, and based on Federal Republic of Germany patent application no. DE 101 53 344.6, 15 filed October 29, 2001.

Field of the Invention

The present invention relates to substituted pyrazolopyrimidines and thiazolopyrimidines, processes for 20 their preparation, substance libraries containing them, medicaments that contain these compounds, the use of these compounds for the production of medicaments for the treatment and/or prophylaxis of pain, epilepsy, schizophrenia, neurodegenerative conditions, in particular 25 Alzheimer's disease, Huntington's disease and Parkinson's disease, cerebral ischaemias and infarcts, psychoses due to raised amino acid levels, cerebral oedemas, insufficiency states of the central nervous system, in particular with hypoxias, especially neonatal hypoxia, and anoxias, AIDS 30 dementia, encephalomyelitis, Tourette's syndrome, perinatal asphyxia, tinnitus, neuropathic pain, respiratory pathway diseases, cancer, cardiac arrhythmias, malfunctions and diseases of the immune system, inflammatory conditions and diseases, neurodegenerative conditions, Parkinson's 35 disease, kidney failure, schizophrenia, sleep disturbances,

strokes, thromboses, urinary incontinence, diabetes, psoriasis, septic shock, cerebral traumas, glaucoma and/or congestive insufficiency, as well as pharmaceutical preparations containing these compounds.

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Background of the Invention

The treatment of chronic and non-chronic pain conditions is very important in medicine. There is therefore a universal need for highly effective therapies for a patient-friendly 10 and targeted treatment of chronic and non-chronic pain conditions, including the successful and satisfactory treatment of pain on the part of the patient.

Conventional opioids such as morphine are highly effective 15 in treating severe to extremely severe pain. Their use is however limited by the known side effects such as for example respiratory depression, vomiting, sedation, constipation and development of tolerance. Also, they are less effective in treating neuropathic or incidental pain 20 afflicting in particular tumour patients.

Opioids exert their analgesic effect by binding to cell membrane receptors that belong to the family of the so-called G protein-coupled receptors. In addition to these there are further receptors as well as ion channels that 25 are significantly involved in the system of pain generation and pain transmission, for example the N-methyl-D-aspartate ion channel (NMDA ion channel), via which a substantial part of synaptic communication proceeds and through which the calcium ion exchange between a neuronal cell and its 30 environment is controlled (see for example P.D. Leeson, L.L. Iversen, *J. Med. Chem.* 37 (1994) 4053-4067).

Important knowledge concerning the physiological importance of ion channel selective substances has been made possible by the development of the patch-clamp technique, by means of which the effect of NMDA antagonists (i.e. antagonists 5 of the NMDA ion channel) on the calcium level in the cell interior can be detected.

In the unactivated state the NMDA ion channels are in each case closed by individual magnesium ions that are present 10 in the interior of the channel and cannot pass through the latter on account of their size. In the activated state the smaller calcium and sodium ions can pass through the channel. The (+)-MK801 binding site of the NMDA ion channel (ionotropic NMDA receptor) is also present in the 15 interior of this membrane protein. Substances with an NMDA antagonistic action, such as phencyclidine (PCP), ketamine or MK801, occupy this binding site (so-called "channel blockers") and accordingly close the relevant NMDA ion channel.

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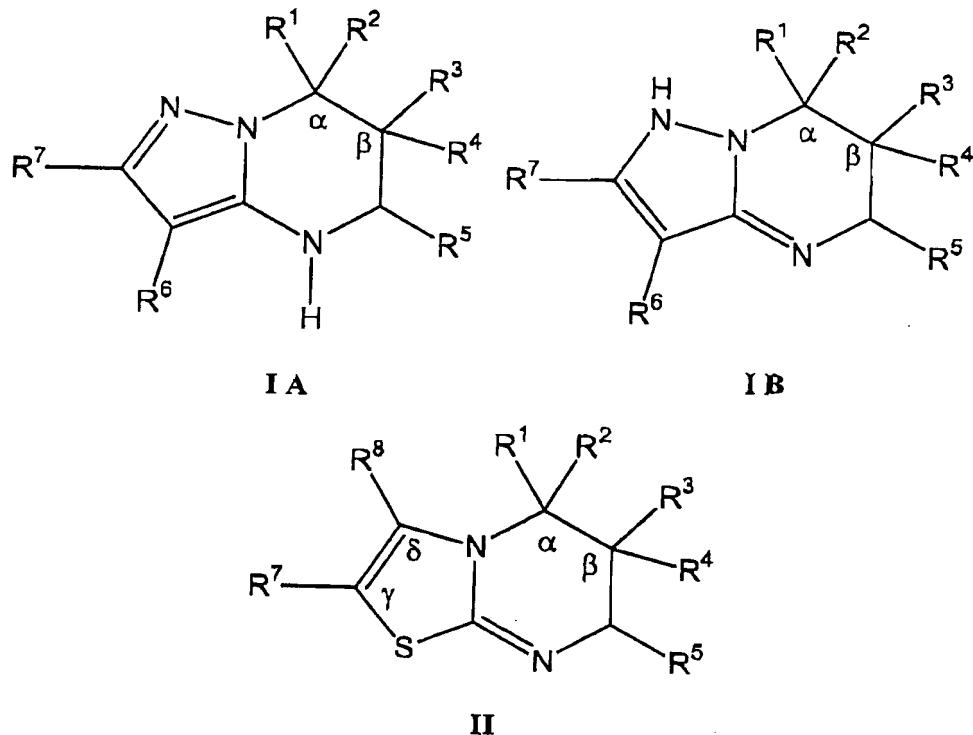
#### Summary of the Invention

One object of the present invention is to provide analgesically active compounds that are suitable for relieving pain and possibly also for relieving chronic and 25 neuropathic pain. In addition these substances should as far as possible produce none of the side effects that normally occur when using opioids such as morphine, for example nausea, vomiting, dependence, respiratory depression or constipation.

30

This object is achieved by the compounds of the general structure (I A), (I B) and (II), which are analgesically active and bind to the MK801 binding site of the NMDA

receptor. The compounds according to the invention are substituted pyrazolopyrimidines and thiazolopyrimidines of the general structure (I A), (I B) or (II)



5 wherein

$R^1$  and  $R^2$  independently of one another denote H,  $O-R^9$ ,  $S-R^{10}$ ,  $C_{1-12}$ -alkyl,  $C_{3-8}$ -cycloalkyl,  $-CH_2-C_{3-8}$ -cycloalkyl, aryl,  $-(C_{1-6}$ -alkyl)-aryl, heterocyclyl or  $-(C_{1-6}$  alkyl)-heterocyclyl,

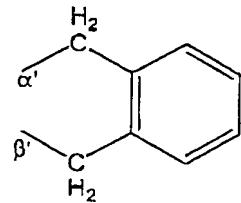
10 in which one of the radicals  $R^1$  and  $R^2$  is H and the other radical of  $R^1$  and  $R^2$  is not H, or in the case that one of the radicals  $R^1$  and  $R^2$  denotes aryl, the other radical of  $R^1$  and  $R^2$  denotes H or  $C_{1-12}$ -alkyl,

15  $R^3$  and  $R^4$  denote H,  $C_{1-12}$ -alkyl,  $C_{3-8}$ -cycloalkyl,  $-CH_2-C_{3-8}-$  cycloalkyl, aryl or  $-(C_{1-6}\text{-alkyl})\text{-aryl}$  in which at least one of the radicals  $R^3$  and  $R^4$  is H, or

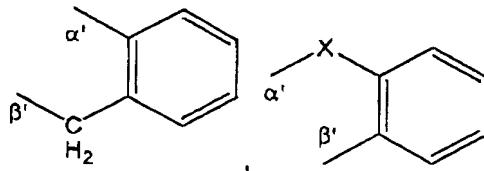
one of the radicals  $R^1$  and  $R^2$  together with one of the radicals  $R^3$  and  $R^4$  forms  $W$ , where  $W$  denotes  $\alpha'-(CH_2)_n-\beta'$  where  $n = 3, 4, 5$  or  $6$ ,  $\alpha'-CH=CH-CH_2-\beta'$ ,  $\alpha'-CH_2-CH=CH-CH_2-\beta'$ ,  $\alpha'-CH_2-CH_2-CH=CH-\beta'$ ,

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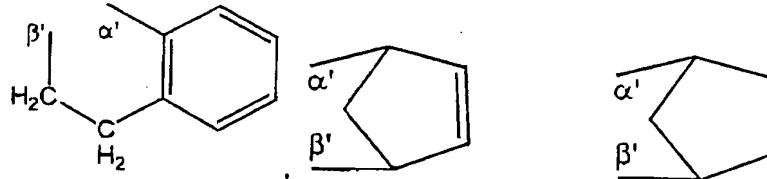
$\alpha'-CH_2-CH_2-CH_2-CH=CH-\beta'$ ,



$\alpha'-O-(CH_2)_m-\beta'$  where  $m = 2, 3, 4$  or  $5$ ,



where  $X = CH_2, O$  or  $S$ ,



or

10

the end of  $W$  identified by  $\alpha'$  is joined to the atom of the compound of the general structure (I A), (I B) or (II) identified by  $\alpha$ , and the end of  $W$  identified by  $\beta'$  is joined to the atom of the compound of the general structure (I A), (I B) or (II) identified by  $\beta$ , the other radical of  $R^1$  and  $R^2$  is H or  $C_{1-12}$ -alkyl, and the other radical of  $R^3$  and  $R^4$  is H or  $C_{1-12}$ -alkyl;

15

$R^5$  denotes  $C_{1-12}$ -alkyl,  $C_{3-8}$ -cycloalkyl,  $-CH_2-C_{3-8}-$  cycloalkyl, aryl,  $-(C_{1-6}$  alkyl)-aryl,

heterocyclyl,  $-(C_{1-6}\text{-alkyl})\text{-heterocyclyl}$  or  
 $C(=O)R^{11}$ ;  
 R<sup>6</sup> denotes H,  $C_{1-8}\text{-alkyl}$ , -CN, fluorine, chlorine,  
 bromine, iodine,  $NO_2$ ,  $NH_2$ ,  $NHR^{12}$ ,  $NR^{13}R^{14}$ ,  $OR^{15}$ ,  
 5  $S(O)_pR^{16}$  where p = 0, 1 or 2,  $-C(=O)R^{17}$  or  
 $-N=N\text{-aryl}$ ;  
 R<sup>7</sup> denotes H,  $C_{1-8}\text{-alkyl}$ , aryl, -CN, fluorine,  
 chlorine, bromine, iodine,  $NO_2$ ,  $NH_2$ ,  $NHR^{12}$ ,  $NR^{13}R^{14}$ ,  
 10  $OR^{18}$ ,  $S(O)_qR^{19}$  where q = 0, 1 or 2 or denotes  
 $C(=O)R^{20}$ ;  
 R<sup>8</sup> denotes H,  $C_{1-8}\text{-alkyl}$  or aryl,  
 or  
 the radicals R<sup>7</sup> and R<sup>8</sup> together form Y, where Y denotes  $\gamma\text{-}$   
 15  $CR^{21}=CR^{22}\text{-}CR^{23}=CR^{24}\text{-}\delta'$  and the end of Y identified by  
 $\gamma'$  is joined to the atom of the general structure  
 $(II)$  identified by  $\gamma$ , and the end of Y identified  
 by  $\delta'$  is joined to the atom of the general  
 structure (II) identified by  $\delta$ ;  
 R<sup>9</sup> and R<sup>10</sup> independently of one another denote H,  $C_{1-8}\text{-alkyl}$ ,  
 20  $C_{3-8}\text{-cycloalkyl}$ ,  $-CH_2\text{-}C_{3-8}\text{-cycloalkyl}$ , aryl or  
 $-(C_{1-6}\text{-alkyl})\text{-aryl}$ ;  
 R<sup>11</sup> denotes H,  $C_{1-8}\text{-alkyl}$ ,  $C_{3-8}\text{-cycloalkyl}$ ,  $-CH_2\text{-}C_{3-8}\text{-}$   
 cycloalkyl, aryl or  $OR^{25}$ ;  
 R<sup>12</sup> denotes  $C_{1-6}\text{-alkyl}$  or  $-CH_2\text{-aryl}$ ;  
 25 R<sup>13</sup> and R<sup>14</sup> are identical or different  $C_{1-6}\text{-alkyl}$  or together  
 denote  $-(CH_2)_h$  where h = 4 or 5;  
 R<sup>15</sup> and R<sup>16</sup> independently of one another denote H,  $C_{1-8}\text{-alkyl}$ ,  
 30  $C_{3-8}\text{-cycloalkyl}$ ,  $-CH_2\text{-}C_{3-8}\text{-cycloalkyl}$ , aryl or  
 $-(C_{1-6}\text{-alkyl})\text{-aryl}$ ;  
 R<sup>17</sup> denotes H,  $C_{1-8}\text{-alkyl}$ ,  $C_{3-8}\text{-cycloalkyl}$ ,  $-CH_2\text{-}C_{3-8}\text{-}$   
 cycloalkyl, aryl,  $-(C_{1-6}\text{-alkyl})\text{-aryl}$ ,  $NH_2$ ,  $NHR^{12}$ ,  
 $NR^{13}R^{14}$  or  $OR^{26}$ ;

$R^{18}$  and  $R^{19}$  independently of one another denote H,  $C_{1-8}$ -alkyl,  $C_{3-8}$ -cycloalkyl,  $-CH_2-C_{3-8}$ -cycloalkyl, aryl or  $-(C_{1-6}$ -alkyl)-aryl;

$R^{20}$  denotes H,  $C_{1-8}$ -alkyl,  $C_{3-8}$ -cycloalkyl,  $-CH_2-C_{3-8}$ -cycloalkyl, aryl or  $-(C_{1-6}$ -alkyl)-aryl or  $OR^{27}$ ;

5  $R^{21}$ ,  $R^{22}$ ,  $R^{23}$  and  $R^{24}$  independently of one another denote H, fluorine, chlorine, bromine, iodine or  $OR^{28}$ ;

$R^{25}$ ,  $R^{26}$ ,  $R^{27}$  and  $R^{28}$  independently of one another denote H or  $C_{1-6}$ -alkyl, where  $R^{25}$  does not denote H if

10 simultaneously  $R^1$  denotes aryl and  $R^2$  denotes alkyl.

#### Detailed Description of the Embodiments

The compounds according to the invention of the general structure (I A), (I B) or (II) in the represented form or in the form of their acid(s) or their base(s) or in the form of one of their salts, in particular one of their physiologically compatible salts, or in the form of one of their solvates, in particular the hydrates; in the form of their racemate, in the form of the pure stereoisomers, in particular enantiomers or diastereomers, or in the form of mixtures of the stereoisomers, in particular of the enantiomers or diastereomers, are present in an arbitrary mixture ratio. The compounds according to the invention, in particular the pyrazolopyrimidines (I) according to the invention, may be present in tautomeric forms, in the case of (I) in the forms (I A) and (I B), wherein the optionally preferred tautomeric form may vary from compound to compound and for example depending on the aggregate state 30 or on the chosen solvent.

The following compounds of the general structure (I A), (I B) or (II) are already known in the prior art, though

their use has not been described in a medicament or for the production of a medicament for the treatment and/or prophylaxis of pain, epilepsy, schizophrenia, neurodegenerative conditions, in particular Alzheimer's disease, Huntington's disease and Parkinson's disease, cerebral ischaemias and infarcts, psychoses due to raised amino acid levels, cerebral oedemas, insufficiency states of the central nervous system, in particular in hypoxias and anoxias, AIDS dementia, encephalomyelitis, Tourette's syndrome, perinatal asphyxia and tinnitus:

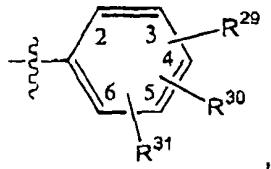
4,5,6,7-tetrahydro-2-methyl-5,7-diphenylpyrazolo[1,5-a]pyrimidine, 4,5,6,7-tetrahydro-2,5-dimethyl-7-phenylpyrazolo[1,5-a]pyrimidine, 4,5,6,7-tetrahydro-5,7-dimethyl-3-phenylpyrazolo[1,5-a]pyrimidine, 4,5,6,7-tetrahydro-2,5,7-trimethylpyrazolo[1,5-a]pyrimidine, 4,5,6,7-tetrahydro-5,7-dimethyl-2-phenylpyrazolo[1,5-a]pyrimidine (B. Koren et al., Tetrahedron (1976) 32, 493-497; 4,5,6,7-tetrahydro-2-methyl-5,7-di-n-propylpyrazolo[1,5-a]pyrimidine-3-carbonitrile, 4,5,6,7-tetrahydro-5-methyl-7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidine-3-carbonitrile, 7-[4-chloro)-phenyl]-4,5,6,7-tetrahydro-5-methylpyrazolo[1,5-a]pyrimidine-3-carbonitrile, 7-[3-chloro)-phenyl]-4,5,6,7-tetrahydro-5-methylpyrazolo[1,5-a]pyrimidine-3-carbonitrile (EP 0 264 773 A1); 3,4-dihydro-2-(4-nitrophenyl)-4-phenyl-2H-pyrimido[2,1-b]benzothiazole, 3,4-dihydro-4-(4-methylphenyl)-2-(4-nitrophenyl)-2H-pyrimido[2,1-b]benzothiazole (M.A. Abdel-Rahman et al., CA (1995) 796768 [Rev. Roum. Chim. (1995) 42, 165-172]).

These compounds are therefore also the subject of the present invention, as are processes according to the invention for their preparation, substance libraries or medicaments containing them, as well as their use for the

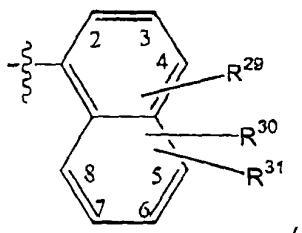
production of medicaments for the treatment and/or prophylaxis of pain, epilepsy, schizophrenia, neurodegenerative conditions, in particular Alzheimer's disease, Huntington's disease and Parkinson's disease,  
5 cerebral ischaemias and infarcts, psychoses due to raised amino acid levels, cerebral oedemas, insufficiency states of the central nervous system, especially in hypoxias and anoxias, AIDS dementia, encephalomyelitis, Tourette's syndrome, perinatal asphyxia and tinnitus, as well as  
10 further medical conditions mentioned in this disclosure.

The terms "alkyl", "C<sub>1-12</sub>-alkyl", "C<sub>1-8</sub>-alkyl" and "C<sub>1-6</sub>-alkyl" include within the scope of the present invention acyclic saturated or unsaturated hydrocarbon radicals that may be  
15 branched or straight-chain as well as unsubstituted or singly substituted or multiply identically or differently substituted with (as in the case of C<sub>1-12</sub>-alkyl) 1 to 12 (i.e. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12), with (as in the case of C<sub>1-12</sub>-alkyl) 1 to 8 (i.e. 1, 2, 3, 4, 5, 6, 7 or  
20 8) or with (as in the case of C<sub>1-6</sub>-alkyl) 1 to 6 (i.e. 1, 2, 3, 4, 5 or 6) C atoms, i.e. C<sub>1-12</sub>-alkanyls, C<sub>1-8</sub>-alkanyls or C<sub>1-6</sub>-alkanyls, C<sub>2-12</sub>-alkenyls, C<sub>2-8</sub>-alkenyls or C<sub>2-6</sub>-alkenyls, and C<sub>2-12</sub>-alkinyls, C<sub>2-8</sub>-alkinyls or C<sub>2-6</sub>-alkinyls. In this connection "alkinyls" have at least one C-C double bond, and  
25 "alkinyls" have at least one C-C triple bond. Preferably alkyl is selected from the group comprising methyl, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, 2-hexyl, n-heptyl, n-octyl, n-nonyl, n-decyl, n-dodecyl; ethenyl  
30 (vinyl), ethinyl, propenyl (-CH<sub>2</sub>CH=CH<sub>2</sub>, -CH=CH-CH<sub>3</sub>, -C(=CH<sub>2</sub>)-CH<sub>3</sub>), propinyl (-CH<sub>2</sub>-C≡CH, -C≡C-CH<sub>3</sub>), butenyl, butinyl, pentenyl, pentinyl, hexenyl, hexinyl, octenyl and octinyl.

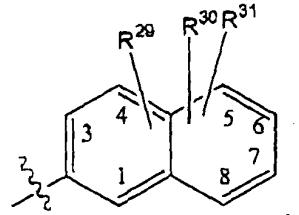
- "C<sub>3-8</sub>-cycloalkyl" (or "cycloalkyl") denotes within the context of the present invention a cyclic saturated or unsaturated hydrocarbon radical with 3, 4, 5, 6, 7 or 8 C atoms, in which the radical may be unsubstituted or singly 5 substituted or multiply identically or differently substituted and may optionally be benzo-condensed.
- Cycloalkyl denotes for example cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclopentenyl, cyclohexenyl, cycloheptenyl and 10 cyclooctenyl. For the purposes of the present invention the following are particularly preferred: cyclopropyl, cyclopropyl-2-carboxylic acid, cyclopropyl-2-carboxylic acid ethyl ester and cyclohexyl.
- 15 For the purposes of the present invention the expression "aryl" is understood to denote a radical that is selected from the group comprising phenyl, naphthyl, anthracenyl and biphenyl, and is unsubstituted or is singly or multiply identically or differently substituted. The aryl radicals 20 may also be condensed with further saturated, (partially) unsaturated or aromatic ring systems. Each aryl radical may be present unsubstituted or singly or multiply substituted, in which the aryl substituents may be identical or different and may be in any arbitrary position 25 of the aryl radical. Advantageously aryl denotes aryl', which includes aryl<sup>1</sup>, aryl<sup>2</sup> and aryl<sup>3</sup>. In this connection aryl<sup>1</sup> denotes



aryl<sup>2</sup> denotes

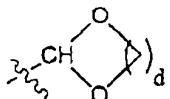


and aryl<sup>3</sup> denotes



wherein R<sup>29</sup>, R<sup>30</sup> and R<sup>31</sup> independently of one another denote

- 5 H, -C<sub>1-6</sub>-alkyl, C<sub>3-8</sub>-cycloalkyl, -(C<sub>1-6</sub> alkyl)-C<sub>3-8</sub>-cycloalkyl, aryl, (C<sub>1-6</sub> alkyl)-aryl, heterocyclyl, -(C<sub>1-6</sub> alkyl)-heterocyclyl, F, Cl, Br, I, -CN, -NC, -OR<sup>32</sup>, -SR<sup>33</sup>, -NO, -NO<sub>2</sub>, NH<sub>2</sub>, NHR<sup>34</sup>, NR<sup>35</sup>R<sup>36</sup>, -N-OH, -N-OC<sub>1-6</sub>-alkyl, -NH<sub>2</sub>, -NHNH<sub>2</sub>, -N=N-aryl, -(C=O)R<sup>37</sup>,



- 10 where d = 1, 2 or 3, or denote -(C=S)R<sup>37</sup>, and may be in any arbitrary ring position;

R<sup>32</sup> and R<sup>33</sup> independently of one another denote H, -C<sub>1-6</sub>-alkyl, -C<sub>3-8</sub>-cycloalkyl, -(C<sub>1-6</sub>-alkyl)-C<sub>3-8</sub>-cycloalkyl, -aryl, -(C<sub>1-6</sub>-alkyl)-aryl, -heterocyclyl, -(C<sub>1-6</sub>-alkyl)-

- 15 heterocyclyl, (C=O)R<sup>38</sup>, -[(CH<sub>2</sub>)<sub>w</sub>-O]<sub>z</sub>-H or -[(CH<sub>2</sub>)<sub>w</sub>-O]<sub>z</sub>-C<sub>1-6</sub>-alkyl where w = 1, 2, 3 or 4 and z = 1, 2, 3, 4 or 5;

R<sup>34</sup> denotes C<sub>1-6</sub>-alkyl, -CH<sub>2</sub>-aryl or -(C=O)O-tert.-butyl;

R<sup>35</sup> and R<sup>36</sup> independently of one another denote C<sub>1-6</sub>-alkyl or together denote -(CH<sub>2</sub>)<sub>-g</sub> where g = 4 or 5;

- 20 R<sup>37</sup> denotes H, -C<sub>1-6</sub>-alkyl, -C<sub>3-8</sub>-cycloalkyl, -(C<sub>1-6</sub>-alkyl)-C<sub>3-8</sub>-cycloalkyl, -aryl, -(C<sub>1-6</sub>-alkyl)-aryl, -heterocyclyl, -(C<sub>1-6</sub>-alkyl)-heterocyclyl, -OR<sup>39</sup>, -NH<sub>2</sub>, -NHR<sup>34</sup>, -NR<sup>35</sup>R<sup>36</sup>;

R<sup>38</sup> denotes H, -C<sub>1-6</sub>-alkyl, -C<sub>3-8</sub>-cycloalkyl, -(C<sub>1-6</sub>-alkyl)-C<sub>3-8</sub>-cycloalkyl, -aryl, -(C<sub>1-6</sub>-alkyl)-aryl; and

$R^{39}$  denotes H, - $C_{1-6}$ -alkyl, - $C_{3-8}$ -cycloalkyl, -( $C_{1-6}$ -alkyl)- $C_{3-8}$ -cycloalkyl, -aryl, -( $C_{1-6}$ -alkyl)-aryl, -heterocyclyl or -( $C_{1-6}$ -alkyl)-heterocyclyl.

Particularly preferred aryl radicals for the purposes of  
5 the invention are phenyl, 3-fluorophenyl, 3-bromophenyl, 4-  
bromophenyl, 4-chlorophenyl, 4-fluorophenyl, 3-  
methylphenyl, 4-methylphenyl, 4-hydroxyphenyl, 4-  
methoxyphenyl, 2,4-dimethylphenyl, 3,4-dimethoxyphenyl,  
10 2,3,4-trimethoxyphenyl, 2-naphthyl, 4-trifluorophenyl, 4-  
phenoxyphenyl, 2-hydroxy-3-methoxyphenyl, 4-hydroxy-3-  
methoxyphenyl and 3-carboxy-2-hydroxyphenyl.

The expression "heterocyclyl" denotes a monocyclic or  
15 polycyclic organic radical in which at least one ring  
contains 1 heteroatom or 2, 3, 4 or 5 identical or  
different heteroatoms that is/are selected from the group  
comprising N, O and S, wherein the radical is saturated or  
unsaturated, and is unsubstituted or singly substituted or  
multiply identically or differently substituted. Examples  
20 of heterocyclyl radicals within the scope of the present  
invention are monocyclic 5-membered, 6-membered or 7-  
membered organic radicals containing 1 heteroatom or 2, 3,  
4 or 5 identical or different heteroatoms that is/are  
nitrogen, oxygen and/or sulfur, and their benzo-condensed  
25 analogues. The "heteroaryl" radicals form a subgroup of the  
heterocyclyl radicals, and comprise those heterocyclyl  
radicals in which the at least one ring that contains the  
heteroatom(s) is heteroaromatic. Each heteroaryl radical  
may be present unsubstituted or singly substituted or  
30 multiply identically or differently substituted. Examples  
of heterocyclyl radicals within the context of the present  
invention are pyrrolidinyl, tetrahydrofuryl, piperidinyl,  
piperazinyl and in particular morpholinyl. Examples of

heterocyclyl radicals that are at the same time heteroaryl radicals are pyrrolyl, pyrazolyl, imidazolyl, pyridazinyl, pyrimidinyl, pyrazinyl and in particular furanyl, thieryl and pyridinyl as well as their benzo-condensed analogues.

- 5 All these radicals may in each case be present unsubstituted or singly or multiply, identically or differently substituted.

The expressions "(C<sub>1-6</sub>-alkyl)-C<sub>3-8</sub>-cycloalkyl", "(C<sub>1-6</sub>-alkyl)-heterocyclyl" and "(C<sub>1-6</sub>-alkyl)-aryl" denote, for the purposes of the present invention, that the cycloalkyl, heterocyclyl or aryl radical is bound via a C<sub>1-6</sub>-alkyl group to the compound with which it is substituted. The same comments apply to the expression "CH<sub>2</sub>-C<sub>3-8</sub>-cycloalkyl".

15 In connection with the expressions "alkyl", "alkanyl", "alkenyl", "alkinyl" and "cycloalkyl", the term "substituted" within the meaning of the present invention is understood to mean the replacement of a hydrogen atom by for example F, Cl, Br, I, -CN, -NC, NH<sub>2</sub>, NH-alkyl, NH-aryl, NH-alkyl-aryl, NH-heterocyclyl, NH-alkyl-OH, N(alkyl)<sub>2</sub>, N(alkyl-aryl)<sub>2</sub>, N(heterocyclyl)<sub>2</sub>, N(alkyl-OH)<sub>2</sub>, NO, NO<sub>2</sub>, SH, S-alkyl, S-aryl, S-alkyl-aryl, S-heterocyclyl, S-alkyl-OH, S-alkyl-SH, OH, O-alkyl, O-aryl, O-alkyl-aryl, O-heterocyclyl, O-alkyl-OH, CHO, C(=O)C<sub>1-6</sub>-alkyl, C(=S)C<sub>1-6</sub>-alkyl, C(=O)aryl, C(=S)aryl, C(=O)C<sub>1-6</sub>-alkyl-aryl, C(=S)C<sub>1-6</sub>-alkyl-aryl, C(=O)-heterocyclyl, C(=S)-heterocyclyl, CO<sub>2</sub>H, CO<sub>2</sub>-alkyl, CO<sub>2</sub>-alkyl-aryl, C(=O)NH<sub>2</sub>, C(=O)NH-alkyl, C(=O)NH-aryl, C(=O)NH-heterocyclyl, C(=O)N(alkyl)<sub>2</sub>, C(=O)N(alkyl-aryl)<sub>2</sub>, C(=O)N(heterocyclyl)<sub>2</sub>, SO-alkyl, SO<sub>2</sub>-alkyl, SO<sub>2</sub>-alkyl-aryl, SO<sub>2</sub>NH<sub>2</sub>, SO<sub>3</sub>H, SO<sub>3</sub>-alkyl, cycloalkyl, aryl or heterocyclyl, in which multiply substituted radicals are understood to mean those radicals that are multiply substituted, e.g. doubly

or triply substituted, either on different atoms or on the same atom, for example triply substituted on the same C atom as in the case of  $\text{CF}_3$  or  $-\text{CH}_2\text{CF}_3$ , or at different positions, as in the case of  $-\text{CH}(\text{OH})-\text{CH}=\text{CCl}-\text{CH}_2\text{Cl}$ . The 5 multiple substitution may be carried out with the same or with different substituents. Particularly preferred for the purposes of the present invention are  $\text{CF}_3$  and  $\text{CH}_2-\text{CH}_2-\text{OH}$  as substituted alkyl as well as cyclopropyl-2-carboxylic acid and cyclopropyl-2-carboxylic acid ethyl ester as 10 substituted cycloalkyl.

With reference to "aryl", "heterocyclyl" as well as "heteroaryl", within the context of the present invention the term "singly substituted" or "multiply substituted" is 15 understood to denote the single or multiple substitution, e.g. double, triple or fourfold substitution, of one or more hydrogen atoms of the ring system by a suitable substituent. Insofar as the meaning of this suitable substituent in connection with "aryl", "heterocyclyl" or 20 "heteroaryl" is not defined in another place in the description or in the claims, suitable substituents are F, Cl, Br, I,  $-\text{CN}$ ,  $-\text{NC}$ ,  $\text{NH}_2$ ,  $\text{NH-alkyl}$ ,  $\text{NH-aryl}$ ,  $\text{NH-alkyl-aryl}$ ,  $\text{NH-heterocyclyl}$ ,  $\text{NH-alkyl-OH}$ ,  $\text{N(alkyl)}_2$ ,  $\text{N(alkyl-aryl)}_2$ ,  $\text{N(heterocyclyl)}_2$ ,  $\text{N(alkyl-OH)}_2$ ,  $\text{NO}$ ,  $\text{NO}_2$ ,  $\text{SH}$ ,  $\text{S-alkyl}$ , 25  $\text{S-cycloalkyl}$ ,  $\text{S-aryl}$ ,  $\text{S-alkyl-aryl}$ ,  $\text{S-heterocyclyl}$ ,  $\text{S-alkyl-OH}$ ,  $\text{S-alkyl-SH}$ ,  $\text{OH}$ ,  $\text{O-alkyl}$ ,  $\text{O-cycloalkyl}$ ,  $\text{O-aryl}$ ,  $\text{O-alkyl-aryl}$ ,  $\text{O-heterocyclyl}$ ,  $\text{O-alkyl-OH}$ ,  $\text{CHO}$ ,  $\text{C(=O)C}_{1-6}\text{-alkyl}$ ,  $\text{C(=S)C}_{1-6}\text{-alkyl}$ ,  $\text{C(=O)aryl}$ ,  $\text{C(=S)aryl}$ ,  $\text{C(=O)C}_{1-6}\text{-alkyl-aryl}$ ,  $\text{C(=S)C}_{1-6}\text{-alkyl-aryl}$ ,  $\text{C(=O)-heterocyclyl}$ ,  $\text{C(=S)-heterocyclyl}$ ,  $\text{CO}_2\text{H}$ ,  $\text{CO}_2\text{-alkyl}$ ,  $\text{CO}_2\text{-alkyl-aryl}$ ,  $\text{C(=O)NH}_2$ ,  $\text{C(=O)NH-alkyl}$ ,  $\text{C(=O)NH-aryl}$ ,  $\text{C(=O)NH-heterocyclyl}$ ,  $\text{C(=O)N(alkyl)}_2$ ,  $\text{C(=O)N(alkyl-aryl)}_2$ ,  $\text{C(=O)N(heterocyclyl)}_2$ ,  $\text{S(O)-alkyl}$ ,  $\text{S(O)-aryl}$ ,  $\text{SO}_2\text{-alkyl}$ ,  $\text{SO}_2\text{-aryl}$ ,  $\text{SO}_2\text{NH}_2$ ,  $\text{SO}_3\text{H}$ ,

CF<sub>3</sub>, =O, =S,; alkyl, cycloalkyl, aryl and/or heterocyclyl; on one or optionally various atoms (in which connection a substituent may optionally in turn be substituted). The multiple substitution is performed with the same or with 5 different substituents.

"Benzo-condensed" denotes for the purposes of the present invention that a benzene ring is condensed onto another ring.

10

Pharmaceutically acceptable or physiologically compatible salts within the context of the present invention are those salts of the compounds according to the invention according to the general structure (I A), (I B) and/or (II) that when 15 used for pharmaceutical purposes, especially in mammals and/or humans, are physiologically compatible. Such pharmaceutically acceptable salts may be formed for example with inorganic or organic acids, or in the case where the compounds according to the invention are carboxylic acids, 20 may be formed with bases.

Preferably the pharmaceutically acceptable salts of the compounds according to the invention according to the general structure (I A), (I B) or (II) are formed with 25 hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, p-toluenesulfonic acid, carbonic acid, formic acid, acetic acid, oxalic acid, succinic acid, tartaric acid, mandelic acid, fumaric acid, lactic acid, citric acid, glutamic acid or aspartic acid. 30 If the compounds according to the invention are carboxylic acids, the pharmaceutically acceptable salts may also be formed by reaction with bases, such as for example sodium hydrogen carbonate or sodium carbonate. The salts that are

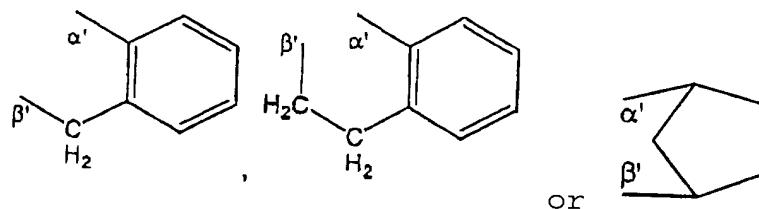
- formed include, *inter alia*, hydrochlorides, hydrobromides, phosphates, carbonates, hydrogen carbonates, formates, acetates, oxalates, succinates, tartrates, fumarates, citrates and glutamates or sodium salts. Particularly
- 5 preferred are the hydrochlorides. Also preferred are the hydrates of the compounds according to the invention, which may be obtained for example by crystallisation from aqueous solution.
- 10 All compounds according to the invention contain at least one asymmetry centre, namely the carbon atom of the structure (I A), (I B) or (II) substituted by R<sup>5</sup>. Accordingly the compounds according to the invention according to the general structure (I A), (I B) or (II) may
- 15 be present in the form of their racemates, in the form of the pure enantiomers and/or diastereomers or in the form of mixtures of these enantiomers and/or diastereomers, and more specifically both as the substance *per se* as well as pharmaceutically acceptable salts of these compounds. The
- 20 mixtures may be present in any arbitrary mixture ratio of the stereoisomers. Preferably the compounds of the general structure (I A), (I B) or (II) are present as enantiomer-pure compounds.
- 25 Preferred are those compounds of the general formulae (I A), (I B) or (II) or their pharmaceutically acceptable salts in which R<sup>1</sup> and R<sup>2</sup> independently of one another denote H, O-R<sup>9</sup>, S-R<sup>10</sup>, C<sub>1-6</sub>-alkyl, aryl' or -(C<sub>1-6</sub>-alkyl)-aryl', wherein
- 30 the aryl' substituents R<sup>29</sup>, R<sup>30</sup> and R<sup>31</sup> independently of one another denote H, C<sub>1-6</sub>-alkyl, F, Cl, Br, I, OH, O-C<sub>1-6</sub>-alkyl, O-aryl<sup>1</sup> or O-CH<sub>2</sub>-aryl<sup>1</sup>,

wherein one of the radicals  $R^1$  and  $R^2$  is H and the other radical of  $R^1$  and  $R^2$  is not H, or in the case that one of the radicals  $R^1$  and  $R^2$  denotes aryl', the other radical of  $R^1$  and  $R^2$  denotes H or  $C_{1-6}$ -alkyl,

5

$R^3$  and  $R^4$  denote H, unsubstituted or singly substituted or multiply identically or differently substituted methyl, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-amyl, isoamyl, sec.-amyl, n-hexyl, isoheptyl, sec.-hexyl, aryl' or  $-CH_2$ -aryl', wherein at least one of the radicals  $R^3$  and  $R^4$  is H, or one of the radicals  $R^1$  and  $R^2$  together with one of the radicals  $R^3$  and  $R^4$  forms W, where W denotes  $\alpha'$ - $CH=CH-CH_2-\beta'$ ,  $\alpha'-CH=CH-CH_2-CH_2-\beta'$ ,  $\alpha'-O-(CH_2)_m-\beta'$  where  $m = 2, 3, 4$  or  $5$ ,

15



the end of W identified by  $\alpha'$  is joined to the atom of the compound of the general structure (I A), (I B) or (II) identified by  $\alpha$ , and the end of W identified by  $\beta'$  is joined to the atom of the general structure (I A), (I B) or (II) identified by  $\beta$ , the other radical of  $R^1$  and  $R^2$  is H or methyl, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-amyl, isoamyl, sec.-amyl, n-hexyl, isoheptyl or sec.-hexyl and the other radical of  $R^3$  and  $R^4$  denotes H or methyl, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-amyl,

20

25

isoamyl, sec.-amyl, n-hexyl, isohexyl, sec.-hexyl;

R<sup>5</sup> denotes methyl, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-amyl, isoamyl, sec.-amyl, n-hexyl, isohexyl, sec.-hexyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl that in each case is unsubstituted or singly substituted or multiply identically or differently substituted, or

10 denotes aryl' or -(CH<sub>2</sub>)<sub>k</sub>-aryl', where k = 1,2,3 or 4, heterocyclyl or C(=O)R<sup>11</sup>;

R<sup>6</sup> denotes H, methyl, ethyl, -CN, fluorine, chlorine, bromine, iodine, -C(=O)R<sup>17</sup> or -N=N-aryl<sup>1</sup>;

15 R<sup>7</sup> denotes H, aryl<sup>1</sup>, OR<sup>18</sup>, S(O)<sub>q</sub>R<sup>19</sup>, where q = 0, 1 or 2, or denotes unsubstituted or singly substituted or multiply identically or differently substituted methyl, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl, n-amyl, isoamyl, sec.-amyl, n-hexyl, isohexyl or sec.-hexyl,

20 R<sup>8</sup> denotes H or aryl',  
or

the radicals R<sup>7</sup> and R<sup>8</sup> together form Y, where Y denotes  $\gamma'$ -CR<sup>21</sup>=CR<sup>22</sup>-CR<sup>23</sup>=CR<sup>24</sup>- $\delta'$  and the end of Y identified by  $\gamma'$  is joined to the atom of the general structure (II) identified by  $\gamma$ , and the end of Y identified by  $\delta'$  is joined to the atom of the general structure (II) identified by  $\delta$ ;

30 R<sup>9</sup> denotes unsubstituted or singly substituted or multiply identically or differently substituted methyl, ethyl, n-propyl, 2-propyl, n-butyl,

isobutyl, sec.-butyl, tert.-butyl, n-amyl,  
 isoamyl, sec.-amyl, n-hexyl, isohexyl, sec.-  
 hexyl, cyclopropyl, cyclobutyl, cyclopentyl,  
 cyclohexyl or cycloheptyl or denotes  $-[(CH_2)_r-O]_s-$   
 H where  $r = 1, 2, 3, 4, 5$  or  $6$  and  $s = 1, 2, 3,$   
 $4, 5$  or  $6$ ;

5       $R^{10}$       denotes aryl';

$R^{11}$       denotes aryl' or  $OR^{25}$ ;

$R^{17}$       denotes  $OR^{26}$ ;

10      $R^{18}$       denotes H or methyl;

$R^{19}$       denotes H, aryl<sup>1</sup>, or in each case unsubstituted,  
                  singly substituted or multiply identically or  
                  differently substituted methyl, ethyl, n-propyl,  
                  2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-  
 15       butyl, n-amyl, isoamyl, sec.-amyl, n-hexyl,  
                  isohexyl or sec.-hexyl;

$R^{21}$ ,  $R^{22}$ ,  $R^{23}$  and  $R^{24}$  independently of one another denote H,  
                  fluorine, chlorine, bromine, iodine or  $OR^{28}$ ;

$R^{25}$       denotes H, methyl, ethyl, n-propyl, 2-propyl, n-  
 20       butyl, isobutyl, sec.-butyl, tert.-butyl, n-amyl,  
                  isoamyl, sec.-amyl, n-hexyl, isohexyl or sec.-  
                  hexyl, where  $R^{25}$  does not denote H if at the same  
                  time  $R^1$  denotes aryl and  $R^2$  denotes alkyl;

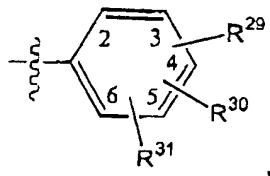
$R^{26}$       denotes H, methyl, ethyl, n-propyl, 2-propyl, n-  
 25       butyl, isobutyl, sec.-butyl, tert.-butyl, n-amyl,  
                  isoamyl, sec.-amyl, n-hexyl, isohexyl or sec.-  
                  hexyl; and

$R^{28}$       denotes H, methyl or ethyl;

    Heterocyclyl denotes furan-2-yl, furan-3-yl, thien-2-yl,  
 30       thien-3-yl, pyridin-2-yl, pyridin-3-yl or  
                  pyridin-4-yl, where furanyl, thiényl and  
                  pyridinyl are in each case unsubstituted or

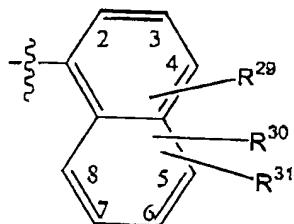
singly substituted or multiply identically or differently substituted;

Aryl' denotes aryl<sup>1</sup>, aryl<sup>2</sup> or aryl<sup>3</sup>;  
Aryl<sup>1</sup> denotes

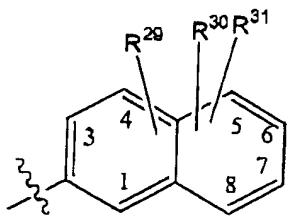


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Aryl<sup>2</sup> denotes

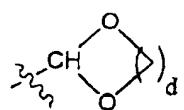


Aryl<sup>3</sup> denotes



10 R<sup>29</sup>, R<sup>30</sup> and R<sup>31</sup> independently of one another denote H, C<sub>1-6</sub>-alkyl, C<sub>3-8</sub>-cycloalkyl, (C<sub>1-6</sub> alkyl)-C<sub>3-8</sub>-cycloalkyl, aryl, (C<sub>1-6</sub>-alkyl)-aryl, heterocyclyl, (C<sub>1-6</sub> alkyl)-heterocyclyl, F, Cl, Br, I, -CN, -NC, -OR<sup>32</sup>, -SR<sup>33</sup>, -NO, -NO<sub>2</sub>, NH<sub>2</sub>, NHR<sup>34</sup>, NR<sup>35</sup>R<sup>36</sup>, -N-OH, -N-OC<sub>1-6</sub>-alkyl, -NHNH<sub>2</sub>, -N=N-aryl, -(C=O)R<sup>37</sup>,

15



where d = 1, 2 or 3, or denotes -(C=S)R<sup>37</sup>, and may be in any arbitrary ring position;

20 R<sup>32</sup> and R<sup>33</sup> independently of one another denote H, -C<sub>1-6</sub>-alkyl, -C<sub>3-8</sub>-cycloalkyl, -(C<sub>1-6</sub>-alkyl)-C<sub>3-8</sub>-cycloalkyl, -aryl, -(C<sub>1-6</sub>-alkyl)-aryl,

-heterocyclyl, -( $C_{1-6}$ -alkyl)-heterocyclyl,  
 $(C=O)R^{38}$ , -[( $CH_2$ )<sub>w</sub>-O]<sub>z</sub>-H or -[( $CH_2$ )<sub>w</sub>-O]<sub>z</sub>- $C_{1-6}$ -alkyl  
 where  $w = 1, 2, 3$  or  $4$  and  $z = 1, 2, 3, 4$  or  $5$ ;  
 5  $R^{34}$  denotes  $C_{1-6}$ -alkyl, - $CH_2$ -aryl or -( $C=O$ )O-tert.-butyl;  
 $R^{35}$  and  $R^{36}$  independently of one another denote  $C_{1-6}$ -alkyl or together denote -( $CH_2$ )<sub>g</sub> where  $g = 4$  or  $5$ ;  
 10  $R^{37}$  denotes H, - $C_{1-6}$ -alkyl, - $C_{3-8}$ -cycloalkyl, -( $C_{1-6}$ -alkyl)- $C_{3-8}$ -cycloalkyl, -aryl, -( $C_{1-6}$ -alkyl)-aryl, -heterocyclyl, -( $C_{1-6}$ -alkyl)-heterocyclyl, -OR<sup>39</sup>, -NH<sub>2</sub>, -NHR<sup>34</sup>, -NR<sup>35</sup>R<sup>36</sup>;  
 15  $R^{38}$  denotes H, - $C_{1-6}$ -alkyl, - $C_{3-8}$ -cycloalkyl, -( $C_{1-6}$ -alkyl)- $C_{3-8}$ -cycloalkyl, -aryl, -( $C_{1-6}$ -alkyl)-aryl; and  
 $R^{39}$  denotes H, - $C_{1-6}$ -alkyl, - $C_{3-8}$ -cycloalkyl, -( $C_{1-6}$ -alkyl)- $C_{3-8}$ -cycloalkyl, -aryl, -( $C_{1-6}$ -alkyl)-aryl, -heterocyclyl or -( $C_{1-6}$ -alkyl)-heterocyclyl.

Among these compounds those are particularly preferred in  
 20 which

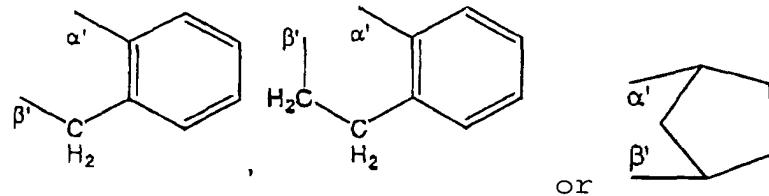
$R^1$  and  $R^2$  independently of one another denote H, O-R<sup>9</sup>, S-R<sup>10</sup>, unsubstituted or singly substituted or multiply identically or differently substituted methyl, ethyl, n-propyl, 2-propyl, n-butyl,  
 25 tert.-butyl or n-hexyl, aryl' or - $CH_2$ -aryl', where the aryl' substituents R<sup>29</sup>, R<sup>30</sup> and R<sup>31</sup> independently of one another denote H, methyl, ethyl, 2-propyl, n-butyl, tert.-butyl, n-hexyl, F, Cl, Br, I, OH, O-methyl, O-ethyl,  
 30 wherein one of the radicals  $R^1$  and  $R^2$  is H and the other radical of  $R^1$  and  $R^2$  is not H, or in the case that one of the radicals  $R^1$  and  $R^2$  denotes aryl', the other radical of  $R^1$  and  $R^2$  denotes H or

methyl, ethyl, n-propyl, 2-propyl, n-butyl,  
tert.-butyl or n-hexyl,

$R^3$  and  $R^4$  denote H, methyl or aryl<sup>1</sup>, wherein the aryl<sup>1</sup> substituents  $R^{29}$ ,  $R^{30}$  and  $R^{31}$  independently of one another are H, methyl or O-methyl,  
5 wherein at least one of the radicals  $R^3$  and  $R^4$  is H,

or

one of the radicals  $R^1$  and  $R^2$  together with one of the 10 radicals  $R^3$  and  $R^4$  forms W, where W denotes  $\alpha'$ -  
 $CH=CH-CH_2-\beta'$ ,  $\alpha'-CH=CH-CH_2-CH_2-\beta'$ ,  $\alpha'-O-(CH_2)_m-\beta'$ , where  
 $m = 2, 3, 4$  or 5



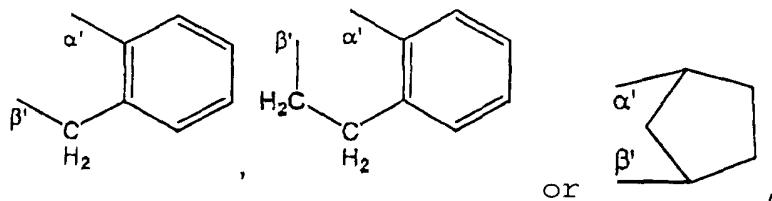
the end of W identified by  $\alpha'$  is joined to the atom of the compound of the general structure

15 (I A), (I B) or (II) identified by  $\alpha$ , and the end of W identified by  $\beta'$  is joined to the atom of the compound of the general structure (I A), (I B) or (II) identified by  $\beta$ , the other radical of  $R^1$  and  $R^2$  and the other radical of  $R^3$  and  $R^4$  in each case 20 denotes H;

$R^5$  denotes methyl, ethyl, n-propyl, 2-propyl, n-butyl, isobutyl, sec.-butyl, tert.-butyl,  $-(CH_2)_4-OH$ , cyclopropyl, where cyclopropyl is unsubstituted or singly substituted by  $C(=O)OH$ , 25  $C(=O)O$ -methyl or  $C(=O)O$ -ethyl, or denotes cyclopentyl, cyclohexyl, aryl<sup>1</sup> or  $-(CH_2)_k$ -aryl<sup>1</sup> where the aryl<sup>1</sup> substituents  $R^{29}$ ,  $R^{30}$  and  $R^{31}$  independently of one another denote H, OH,  $-O-$

methyl,  $\text{O-C}_6\text{H}_5$ ,  $\text{CH}_3$ ,  $\text{CF}_3$  or  $\text{C(=O)OH}$  and  $k = 1$  or  $2$ ,  
 or denotes heterocyclyl or  $\text{C(=O)R}^{11}$ ;  
 $\text{R}^6$  denotes  $\text{H}$ ,  $-\text{CN}$ , bromine,  $-\text{C(=O)R}^{17}$  or  $-\text{N=N-phenyl}$ ;  
 $\text{R}^7$  denotes  $\text{H}$ , aryl<sup>1</sup> where  $\text{R}^{29}$ ,  $\text{R}^{30}$  and  $\text{R}^{31}$  are  $\text{H}$ ,  $\text{OH}$ ,  
 5  $\text{S(O)}_q\text{R}^{19}$ , where  $q = 0$  or  $2$ , or denotes methyl,  
 ethyl, n-propyl, 2-propyl, n-butyl, isobutyl,  
 sec.-butyl or tert.-butyl,  
 $\text{R}^8$  denotes  $\text{H}$ , aryl<sup>1</sup> where the aryl<sup>1</sup> substituents  $\text{R}^{29}$ ,  
 $\text{R}^{30}$  and  $\text{R}^{31}$  independently of one another are  $\text{H}$ ,  
 10 methyl or chlorine, or denotes aryl<sup>3</sup> where  $\text{R}^{29}$ ,  $\text{R}^{30}$   
 and  $\text{R}^{31}$  are  $\text{H}$ ,  
 or  
 the radicals  $\text{R}^7$  and  $\text{R}^8$  together form  $\text{Y}$ , where  $\text{Y}$   
 denotes  $\gamma'\text{-CR}^{21}=\text{CR}^{22}-\text{CR}^{23}=\text{CR}^{24}-\delta'$  and the end of  $\text{Y}$   
 15 identified by  $\gamma'$  is joined to the atom of the  
 general structure (II) identified by  $\gamma$ , and the  
 end of  $\text{Y}$  identified by  $\delta'$  is joined to the atom of  
 the general structure (II) identified by  $\delta$ ;  
 $\text{R}^9$  denotes methyl, ethyl, n-propyl, 2-propyl, n-  
 20 butyl, isobutyl, sec.-butyl, tert.-butyl, n-amyl,  
 isoamyl, sec.-amyl, n-hexyl, isohexyl, sec.-  
 hexyl, cyclopropyl, cyclopentyl or cyclohexyl or  
 denotes  $-[(\text{CH}_2)_r-\text{O}]_s-\text{H}$  where  $r = 1$ ,  $2$  or  $3$  and  $s =$   
 1 or  $2$ ;  
 25  $\text{R}^{10}$  denotes aryl<sup>1</sup>;  
 $\text{R}^{11}$  denotes aryl<sup>1</sup> where  $\text{R}^{29}$ ,  $\text{R}^{30}$  and  $\text{R}^{31}$  denote  $\text{H}$  or  
 $\text{OR}^{25}$ ;  
 $\text{R}^{17}$  denotes  $\text{OR}^{26}$ ;  
 $\text{R}^{19}$  denotes methyl or aryl<sup>1</sup>, where one of the aryl<sup>1</sup>  
 30 substituents  $\text{R}^{29}$ ,  $\text{R}^{30}$  and  $\text{R}^{31}$  is  $\text{H}$  or  $-\text{NO}_2$ , and the  
 two other aryl<sup>1</sup> substituents of  $\text{R}^{29}$ ,  $\text{R}^{30}$  and  $\text{R}^{31}$  are  
 $\text{H}$ ;  
 $\text{R}^{21}$  and  $\text{R}^{23}$  denote  $\text{H}$ ;

R<sup>22</sup> denotes H, fluorine or OR<sup>28</sup>;  
 R<sup>24</sup> denotes H or chlorine;  
 R<sup>25</sup> denotes H, methyl or ethyl, where R<sup>25</sup> does not  
       denote H if at the same time R<sup>1</sup> denotes aryl and  
 5           R<sup>2</sup> denotes alkyl;  
 R<sup>26</sup> denotes H, methyl or ethyl;  
 R<sup>28</sup> denotes methyl or ethyl; and  
 Heterocyclyl denotes furan-2-yl, furan-3-yl, thien-2-yl,  
       thien-3-yl, pyridin-2-yl, pyridin-3-yl or  
 10        pyridin-4-yl, where furanyl, thienyl and  
           pyridinyl are in each case unsubstituted or  
           singly substituted or multiply identically or  
           differently substituted by -NO<sub>2</sub>, -CH<sub>3</sub> or C(=O)OH.  
 Most particularly preferred compounds according to the  
 15 invention of the general structure (I A), (I B) or (II) are  
       those in which  
 R<sup>1</sup> and R<sup>1</sup> independently of one another denote H, O-CH<sub>2</sub>-CH<sub>2</sub>-  
       OH, O-cyclohexyl, S-phenyl, methyl, phenyl, 3-  
       fluorophenyl, 3-bromophenyl, 4-bromophenyl, 4-  
 20        chlorophenyl, 4-fluorophenyl, 3-methylphenyl, 4-  
       hydroxyphenyl, 4-methoxyphenyl, 2,4-  
       dimethylphenyl, 3,4-dimethoxyphenyl, 2,3,4-  
       trimethoxyphenyl, 2-naphthyl or -CH<sub>2</sub>-phenyl,  
 R<sup>3</sup> and R<sup>4</sup> denote H, methyl or 4-methoxyphenyl, where at  
 25        least one of the radicals R<sup>3</sup> and R<sup>4</sup> is H,  
       or  
       one of the radicals R<sup>1</sup> and R<sup>2</sup> together with one of the  
       radicals R<sup>3</sup> and R<sup>4</sup> form W, where W denotes  $\alpha'$ -  
       CH=CH-CH<sub>2</sub>- $\beta'$ ,  $\alpha'$ -CH=CH-CH<sub>2</sub>-CH<sub>2</sub>- $\beta'$ ,  $\alpha'$ -O-(CH<sub>2</sub>)<sub>m</sub>- $\beta'$  where  
 30        m = 2, 3, 4 or 5,



the end of W identified by  $\alpha'$  is joined to the atom of the compound of the general structure (I A), (I B) or (II) identified by  $\alpha$ , and the end of W identified by  $\beta'$  is joined to the atom of the compound of the general structure (I A), (I B) or (II) identified by  $\beta$ , and the other radical of  $R^1$  and  $R^2$  and the other radical of  $R^3$  and  $R^4$  in each case denote H;

5  $R^5$  denotes n-propyl, n-butyl, tert.-butyl,  $-(CH_2)_4-$

10  $OH$ , cyclopropyl, cycloprop-2-yl-1-carboxylic acid ethyl ether, cyclohexyl, 4-trifluorophenyl, 4-phenoxypyphenyl, 2-hydroxy-3-methoxyphenyl, 4-hydroxy-3-methoxyphenyl, 3-carboxy-2-hydroxyphenyl,  $-(CH_2)_2$ -phenyl, 5-carboxyfuran-2-yl, 5-methylfuran-2-yl, 5-nitrofuran-2-yl, 5-nitrothien-2-yl, pyridin-2-yl, pyridin-3-yl,  $C(=O)-$ phenyl,  $C(=O)OH$  or  $C(=O)Oethyl$ , where  $R^5$  does not denote  $C(=O)OH$  if at the same time  $R^1$  denotes aryl and  $R^2$  denotes alkyl;

15  $R^6$  denotes H, -CN, bromo,  $-C(=O)OH$ ,  $-C(=O)Oethyl$  or  $-N=N-phenyl$ ;

20  $R^7$  denotes H, phenyl, OH, -S-methyl,  $-SO_2-$  (4-nitrophenyl) or tert.-butyl;

25  $R^8$  denotes 4-chlorophenyl, 4-methylphenyl or 2-naphthyl;

or

the radicals  $R^7$  and  $R^8$  together form Y, where Y

denotes  $\gamma'$ -CR<sup>21</sup>=CH-CH=CH- $\delta'$  and the end of Y identified by  $\gamma'$  is joined to the atom of the general structure (II) identified by  $\gamma$ , and the end of Y identified by  $\delta'$  is joined to the atom of the general structure (II) identified by  $\delta$ ; and

5 R<sup>21</sup> denotes fluorine, methoxy or ethoxy.

Exemplary and advantageous compounds of the present invention are selected from the group that comprises

- 10 • 3-bromo-5-(5-nitrofuran-2-yl)-7-m-tolyltetrahydropyrazolo[1,5-a]pyrimidine
- 3-bromo-7-(4-fluorophenyl)-7-methyl-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine
- 3-bromo-7-naphthalin-2-yl-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine
- 15 • 2-(3-bromo-7-m-tolyltetrahydropyrazolo[1,5-a]pyrimidin-5-yl)-cyclopropanecarboxylic acid ethyl ester
- 2-[3-bromo-7-(4-bromophenyl)-tetrahydropyrazolo[1,5-a]pyrimidin-5-yl]-cyclopropanecarboxylic acid ethyl ester
- 20 • 2-(3-bromo-7-naphthalin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidin-5-yl)-cyclopropanecarboxylic acid ethyl ester
- 3-bromo-7-(4-fluorophenyl)-7-methyl-5-(5-methylfuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine
- 25 • 3-bromo-7-(3,4-dimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester
- 3-bromo-7-(4-methoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester
- 30 • 3-bromo-7-(4-methoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester

- 3-bromo-7-(4-methoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid
- 3-bromo-7-(2,4-dimethylphenyl)-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine
- 5 • 3-bromo-7-(4-methoxyphenyl)-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine
- 5,5a,6,8a-tetrahydro-3H-1,4,8b-triaza-as-indacene-3,5-dicarboxylic acid diethyl ester; 5,5a,6,8a-tetrahydro-4H-1,4,8b-triaza-as-indacene-3,5-dicarboxylic acid diethyl ester
- 10 • 2-hydroxy-3-phenylazo-5,5a,6,8a-tetrahydro-3H-1,4,8b-triaza-as-indacene-5-carboxylic acid ethyl ester; 2-hydroxy-3-phenylazo-5,5a,6,8a-tetrahydro-4H-1,4,8b-triaza-as-indacene-5-carboxylic acid ethyl ester
- 15 • 2-tert.-butyl-5,5a,6,8a-tetrahydro-3H-1,4,8b-triaza-as-indacene-5-carboxylic acid ethyl ester; 2-tert.-butyl-5,5a,6,8a-tetrahydro-3H-1,4,8b-triaza-as-indacene-5-carboxylic acid ethyl ester
- 20 • 3-bromo-2-phenyl-5,5a,6,8a-tetrahydro-3H-1,4,8b-triaza-as-indacene-5-carboxylic acid ethyl ester; 3-bromo-2-phenyl-5,5a,6,8a-tetrahydro-4H-1,4,8b-triaza-as-indacene-5-carboxylic acid ethyl ester
- 25 • 7-(2,3,4-trimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-3,5-dicarboxylic acid diethyl ester
- 3-cyano-2-methylsulfanyl-7-(2,3,4-trimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester
- 30 • 2-hydroxy-7-(4-hydroxyphenyl)-6-methyl-3-phenylazo-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester

- 3-bromo-7-(4-hydroxyphenyl)-6-methyl-2-phenyltetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester
- 5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-3,5-dicarboxylic acid diethyl ester; 5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluorene-3,5-dicarboxylic acid diethyl ester
- 2-hydroxy-3-phenylazo-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-5-carboxylic acid ethyl ester; 2-hydroxy-3-phenylazo-5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluorene-5-carboxylic acid ethyl ester
- 7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3,5-dicarboxylic acid diethyl ester
- 3-cyano-2-methylsulfanyl-7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester
- 3-cyano-2-methylsulfanyl-7-(2,3,4-trimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid
- 7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3,5-dicarboxylic acid-3-ethyl ester
- 3-cyano-7-(2,4-dimethylphenyl)-2-methylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester
- 3-cyano-7-(2,4-dimethylphenyl)-tetrahydropyrazolo-[1,5-a]pyrimidine-5-carboxylic acid ethyl ester
- 7-(2,4-dimethylphenyl)-tetrahydropyrazolo-[1,5-a]pyrimidine-3,5-dicarboxylic acid-3-ethyl ester
- 3-bromo-7-(2,4-dimethylphenyl)-2-phenyltetrahydropyrazolo-[1,5-a]pyrimidine-5-carboxylic acid

- 3-cyano-7-(2,4-dimethylphenyl)-2-methylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid
- 3-cyano-7-(2,4-dimethylphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid
- 3-cyano-7-(3,4-dimethoxyphenyl)-2-methylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid
- 7-(2,4-dimethylphenyl)-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 7-(2,4-dimethylphenyl)-5-(5-nitrofuran-2-yl)-3-phenylazotetrahydropyrazolo[1,5-a]pyrimidin-2-ol
- 3-bromo-7-(2,4-dimethylphenyl)-5-(5-nitrofuran-2-yl)-2-phenylazotetrahydropyrazolo[1,5-a]pyrimidine
- 7-(2,4-dimethylphenyl)-2-methylsulfanyl-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 7-(2,4-dimethylphenyl)-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 3-bromo-7-(3,4-dimethoxyphenyl)-5-(5-nitrofuran-2-yl)-2-phenyltetrahydropyrazolo[1,5-a]pyrimidine
- 7-(4-methoxyphenyl)-2-methylsulfanyl-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 7-(2,4-dimethylphenyl)-5-(2-ethoxycarbonylcyclopropyl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 2-[7-(2,4-dimethylphenyl)-2-hydroxy-3-phenylazo-tetrahydropyrazolo[1,5-a]pyrimidin-5-yl]-cyclopropanecarboxylic acid ethyl ester

- 2- [2-tert.-butyl-7- (2,4-dimethylphenyl)tetrahydro-  
pyrazolo[1,5-a]pyrimidin-5-yl]cyclopropane-  
carboxylic acid ethyl ester
- 2- [3-bromo-7- (2,4-dimethylphenyl)-2-phenyltetra-  
5 hydropyrazolo[1,5-a]pyrimidin-5-yl]cyclopropane-  
carboxylic acid ethyl ester
- 2- [3-cyano-7- (2,4-dimethylphenyl)-2-methylsulfanyl-  
10 tetrahydropyrazolo[1,5-a]pyrimidin-5-  
yl]cyclopropanecarboxylic acid ethyl ester
- 5- (2-ethoxycarbonylcyclopropyl)-7- (3-fluorophenyl)-  
tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic  
acid ethyl ester
- 2- [3-bromo-7- (3-bromophenyl)-2-phenyltetrahydro-  
pyrazolo[1,5-a]pyrimidin-5-yl]cyclopropane-  
15 carboxylic acid ethyl ester
- 2- [7- (3-bromophenyl)-3-cyano-2-methylsulfanyl-  
tetrahydropyrazolo[1,5-a]pyrimidin-5-  
yl]cyclopropanecarboxylic acid ethyl ester
- 7- (2,4-dimethylphenyl)-5- (5-nitrothiophen-2-yl)-3-  
20 phenylazotetrahydropyrazolo[1,5-a]pyrimidin-2-ol
- 7- (2,4-dimethylphenyl)-2-methylsulfanyl-5- (5-  
nitrothiophen-2-yl)-tetrahydropyrazolo[1,5-  
a]pyrimidine-3-carbonitrile
- 7- (2,4-dimethylphenyl)-5- (5-nitrothiophen-2-yl)-  
25 tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 7- (3,4-dimethoxyphenyl)-5- (5-nitrothiophen-2-yl)-  
tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic  
acid ethyl ester
- 7- (3,4-dimethoxyphenyl)-5- (5-nitrothiophen-2-yl)-3-  
30 phenylazotetrahydropyrazolo[1,5-a]pyrimidin-2-ol
- 3-bromo-7- (3,4-dimethoxyphenyl)-5- (5-nitrothiophen-  
2-yl)-2-phenyltetrahydropyrazolo[1,5-a]pyrimidine

- 7- (3,4-dimethoxyphenyl) -2-methylsulfanyl-5- (5-nitrothiophen-2-yl) -tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 7- (3,4-dimethoxyphenyl) -5- (5-nitrothiophen-2-yl) -tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 7- (4-methoxyphenyl) -5- (5-nitrothiophen-2-yl) -tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 5- [3-bromo-7- (4-methoxyphenyl) -2-phenyltetrahydro-pyrazolo[1,5-a]pyrimidin-5-yl] -furan-2-carboxylic acid
- 5-benzoyl-7- (2,4-dimethylphenyl) -tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 5-benzoyl-7- (2,4-dimethylphenyl) -2-methylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5-benzoyl-7- (2,4-dimethylphenyl) -tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5-benzoyl-7- (3,4-dimethoxyphenyl) -tetrahydro-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- [3-bromo-7- (3,4-dimethoxyphenyl) -2-phenyltetrahydro-pyrazolo[1,5-a]pyrimidin-5-yl] -phenylmethanone
- 5-benzoyl-7- (3,4-dimethoxyphenyl) -2-methylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5-benzoyl-7- (3,4-dimethoxyphenyl) tetrahydro-pyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5-benzoyl-7- (4-methoxyphenyl) -tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 5-benzoyl-7- (4-methoxyphenyl) -2-methylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile

- 5-benzoyl-7-(4-methoxyphenyl)tetrahydropyrazolo-[1,5-a]pyrimidine-3-carbonitrile
- 5-benzoyl-7-(3-fluorophenyl)-tetrahydropyrazolo-[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 5 • [3-bromo-7-(3-fluorophenyl)-2-phenyltetrahydro-pyrazolo[1,5-a]pyrimidin-5-yl]-phenylmethanone
- [3-bromo-7-(3-bromophenyl)-2-phenyltetrahydro-pyrazolo[1,5-a]pyrimidin-5-yl]-phenylmethanone
- 7-(2,4-dimethylphenyl)-5-(4-phenoxyphenyl)tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 10 • 3-bromo-7-(2,4-dimethylphenyl)-5-(4-phenoxyphenyl)-2-phenyltetrahydropyrazolo[1,5-a]pyrimidine
- 7-(2,4-dimethylphenyl)-2-methylsulfanyl-5-(4-phenoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 15 • 7-(2,4-dimethylphenyl)-5-(4-phenoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 7-(3,4-dimethoxyphenyl)-5-(4-phenoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 20 • 7-(3,4-dimethoxyphenyl)-2-methylsulfanyl-5-(4-phenoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 3-[3-cyano-7-(4-hydroxyphenyl)-6-methyltetrahydro-pyrazolo[1,5-a]pyrimidin-5-yl]-2-hydroxybenzoic acid
- 25 • 3-(3-cyano-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluoren-5-yl)-2-hydroxybenzoic acid; 3-(3-cyano-5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluoren-5-yl)-2-hydroxybenzoic acid
- 30

- 3- (3-cyano-7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidin-5-yl)-2-hydroxybenzoic acid
- 3- [2-tert.-butyl-7- (4-chlorophenyl) -7-methyltetrahydropyrazolo[1,5-a]pyrimidin-5-yl]-2-hydroxybenzoic acid
- 5- (4-hydroxy-3-methoxyphenyl) -7- (4-hydroxyphenyl) -6-methyltetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 5- (4-hydroxy-3-methoxyphenyl) -7- (4-hydroxyphenyl) -6-methyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5- (4-hydroxy-3-methoxyphenyl) -5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-3-carboxylic acid ethyl ester; 5- (4-hydroxy-3-methoxyphenyl) -5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta-[c]fluorene-3-carboxylic acid ethyl ester
- 4- (2-tert.-butyl-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluoren-5-yl) -2-methoxyphenol; 4- (2-tert.-butyl-5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluoren-5-yl) -2-methoxyphenol
- 5- (4-hydroxy-3-methoxyphenyl) -2-methylsulfanyl-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-3-carbonitrile; 5- (4-hydroxy-3-methoxyphenyl) -2-methylsulfanyl-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-3-carbonitrile
- 5- (4-hydroxy-3-methoxyphenyl) -7-phenylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 4- (2-tert.-butyl-7-phenylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidin-5-yl) -2-methoxyphenol

- 4-(3-bromo-2-phenyl-7-phenylsulfanyl-tetrahydro-pyrazolo[1,5-a]pyrimidin-5-yl)-2-methoxyphenol
- 5-(2-hydroxy-3-methoxyphenyl)-7-phenylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 7-(4-chlorophenyl)-5-(2-hydroxy-3-methoxyphenyl)-7-methyltetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 5-(4-hydroxybutyl)-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-3-carbonitrile; 5-(4-hydroxybutyl)-5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluorene-3-carbonitrile
- 5-(4-hydroxybutyl)-2-methylsulfanyl-7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5-(4-hydroxybutyl)-7-phenylsulfanyltetrahydro-pyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 7-(4-chlorophenyl)-5-(4-hydroxybutyl)-7-methyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5-butyl-2-methylsulfanyl-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-3-carbonitrile; 5-butyl-2-methylsulfanyl-5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluorene-3-carbonitrile
- 5-butyl-2-methylsulfanyl-7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5-butyl-7-phenylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5-butyl-7-(4-chlorophenyl)-7-methylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5-cyclopropyl-7-(2,4-dimethylphenyl)-3-phenylazo-tetrahydropyrazolo[1,5-a]pyrimidin-2-ol

- 2-tert.-butyl-5-cyclopropyl-7-(2,4-dimethylphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine
- 5-cyclopropyl-7-(2,4-dimethylphenyl)-2-methyl-sulfanyltetrahydro-pyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 2-tert.-butyl-5-cyclopropyl-7-(3,4-dimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine
- 3-bromo-5-cyclopropyl-7-(3,4-dimethoxyphenyl)-2-phenyltetrahydropyrazolo[1,5-a]pyrimidine
- 5-cyclopropyl-7-(4-methoxyphenol)-tetrahydro-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 5-cyclopropyl-3,5,5a,6,7,11b-hexahydro-1,4,11c-triazacyclopenta[c]phenanthrene-3-carbonitrile
- 7-(2,4-dimethylphenyl)-5-pyridin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 7-(2,4-dimethylphenyl)-3-phenylazo-5-pyridin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidin-2-ol
- 3-bromo-7-(2,4-dimethylphenyl)-2-phenyl-5-pyridin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidine
- 7-(2,4-dimethylphenyl)-2-methylsulfanyl-5-pyridin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 7-(3,4-dimethoxyphenyl)-2-methylsulfanyl-5-phenethyl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 7-(3,4-dimethoxyphenyl)-5-phenethyl-tetrahydro-pyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5-cyclopropyl-7-(2-hydroxyethoxy)-tetrahydro-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester

- 2-(2-tert.-butyl-5-cyclopropyltetrahydropyrazolo-[1,5-a]pyrimidin-7-yloxy)-ethanol
- 5-cyclopropyl-3,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacene-3-carboxylic acid ethyl ester; 5-cyclopropyl-4,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacene-3-carboxylic acid ethyl ester
- 5-cyclopropyl-3-phenylazo-3,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacen-2-ol; 5-cyclopropyl-3-phenylazo-4,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacen-2-ol
- 7-cyclohexyloxy-5-cyclopropyltetrahydropyrazolo-[1,5-a]pyrimidin-3-carboxylic acid ethyl ester
- 7-cyclohexyloxy-5-cyclopropyl-2-methylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidin-3-carbonitrile
- 7-(4-chlorophenyl)-5-cyclohexyltetrahydropyrazolo-[1,5-a]pyrimidin-3-carbonitrile
- 5-cyclohexyl-7-(2-hydroxyethoxy)-tetrahydro-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 5-cyclohexyl-3,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacene-3-carboxylic acid ethyl ester; 5-cyclohexyl-4,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacene-3-carboxylic acid ethyl ester
- 5-cyclohexyl-7-cyclohexyloxytetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 7-(2,4-dimethylphenyl)-3-phenylazo-5-propyl-tetrahydropyrazolo[1,5-a]pyrimidin-2-ol
- 7-(2,4-dimethylphenyl)-2-methylsulfanyl-5-propyl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 5-tert.-butyl-7-(2,4-dimethylphenyl)-tetrahydro-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester

- 2,5-di-tert.-butyl-7-(3,4-dimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine
- 3-bromo-5-tert.-butyl-7-(3,4-dimethoxyphenyl)-2-phenyltetrahydropyrazolo[1,5-a]pyrimidine
- 5 • 2-[3-cyano-6,7-bis-(4-methoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidin-5-yl]-cyclopropanecarboxylic acid ethyl ester
- 3-cyano-6,7-bis-(4-methoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid
- 10 • 4-[3-bromo-6-methyl-2-phenyl-5-(4-trifluoromethylphenyl)-tetrahydropyrazolo[1,5-a]pyrimidin-7-yl]-phenol
- 7-(4-hydroxyphenyl)-6-methyl-2-methylsulfanyl-5-(4-trifluoromethylphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 15 • 7-(4-hydroxyphenyl)-6-methyl-5-(4-trifluoromethylphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 2-(4-nitrophenylsulfonyl)-5-phenylsulfanyl-7-pyridin-2-yl-6,7-dihydro-5H-thiazolo[3,2-a]pyrimidine
- 20 • 3-(4-chlorophenyl)-5-phenylsulfanyl-7-pyridin-2-yl-6,7-dihydro-5H-thiazolo[3,2-a]pyrimidine
- 5-phenylsulfanyl-7-pyridin-2-yl-3-p-tolyl-6,7-dihydro-5H-thiazolo[3,2-a]pyrimidine
- 25 • 7-methoxy-4-phenylsulfanyl-2-pyridin-2-yl-3,4-dihydro-2H-9-thia-1,4a-diazafluorene
- 7-ethoxy-4-phenylsulfanyl-2-pyridin-2-yl-3,4-dihydro-2H-9-thia-1,4a-diazafluorene
- 30 • 7-fluoro-4-phenylsulfanyl-2-pyridin-2-yl-3,4-dihydro-2H-9-thia-1,4a-diazafluorene

- 3-naphthalin-2-yl-5-phenylsulfanyl-7-pyridin-2-yl-6,7-dihydro-5H-thiazolo[3,2-a]pyrimidine
- 7-phenyl-3-phenylazo-5-pyridin-2-yl-3,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-ol
- 5 • 7-phenylsulfanyl-5-pyridin-2-yl-3,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester
- 3-phenylazo-7-phenylsulfanyl-5-pyridin-2-yl-3,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-ol
- 10 • 3-bromo-7-phenylsulfanyl-5-pyridin-2-yl-3,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine
- 7-phenylsulfanyl-5-pyridin-2-yl-3,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 7-(3,4-dimethoxyphenyl)-2-methylsulfanyl-5-pyridin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile
- 15 • 3-bromo-7-(3,4-dimethoxyphenyl)-2-phenyl-5-pyridin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidine
- 3-bromo-7-(3,4-dimethoxyphenyl)-2-phenyl-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester
- 20 • 3-bromo-7-(3,4-dimethoxyphenyl)-5-(5-nitrofuran-2-yl)-2-phenyl-tetrahydropyrazolo[1,5-a]pyrimidine
- 3-cyano-7-(3,4-dimethoxyphenyl)-2-methylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester
- 25 • 3-cyano-7-(3,4-dimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester
- 3-bromo-7-(3,4-dimethoxyphenyl)-2-phenyl-5-pyridin-2-yl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine
- 30

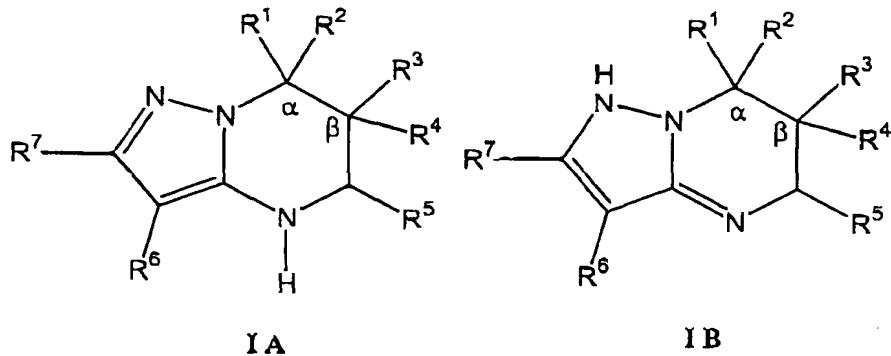
- 7- (3, 4-dimethoxyphenyl)-5-pyridin-2-yl-4, 5, 6, 7-tetrahydropyrazolo[1, 5-a]pyrimidine-3-carbonitrile
  - 7- (3, 4-dimethoxyphenyl)-2-methylsulfanyl-5- (5-nitrofuran-2-yl)-tetrahydropyrazolo[1, 5-a]-pyrimidine-3-carbonitrile
  - 7- (3, 4-dimethoxyphenyl)-5-pyridin-2-yl-4, 5, 6, 7-tetrahydropyrazolo[1, 5-a]pyrimidine-3-carboxylic acid ethyl ester

as well as their pharmaceutically acceptable salts.

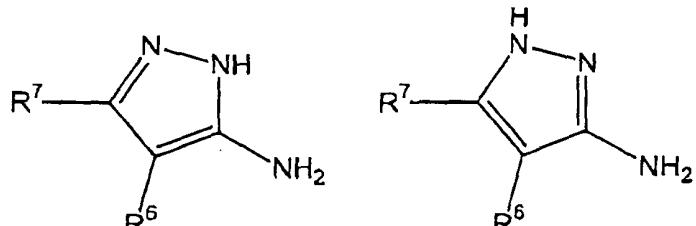
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The present invention also relates to processes for the production of the compounds of the structure (I A), (I B) and (II) according to the invention.

15 Accordingly, the compounds of the general structure (I A) and (I B) as well as their pharmaceutically acceptable salts



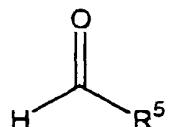
wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are as defined above,  
20 can be prepared by reacting a pyrazolamine of the general  
structure (IIIA) and/or (IIIB)



III A

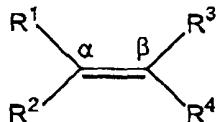
III B

wherein R<sup>6</sup> and R<sup>7</sup> are as defined above, with an aldehyde of the general structure (IV)



IV

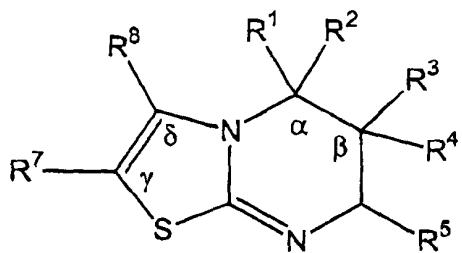
5 wherein R<sup>5</sup> is as defined above, and with an olefin of the general structure (V)



V

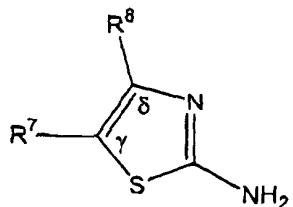
wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are as defined above, with the proviso that if one of the radicals R<sup>1</sup> and R<sup>2</sup> together with 10 one of the radicals R<sup>3</sup> and R<sup>4</sup> forms W, the end of W identified by α' is joined to the α-carbon atom of the olefin of the general structure (V), and the end of W identified by β' is joined to the β-carbon atom of the olefin of the general structure (V), in the presence of an 15 acid.

Accordingly the compounds of the general structure (II) according to the invention as well as their pharmaceutically acceptable salts



II

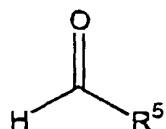
wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^7$  and  $R^8$  are as defined above, can be obtained by reacting a thiazolamine of the general structure (VI)



VI

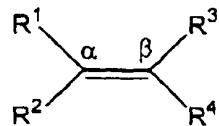
5

wherein  $R^7$  and  $R^8$  are as defined above, with the proviso that if  $R^7$  and  $R^8$  form Y, the end of Y identified by  $\gamma'$  is coupled to the atom of the thiazolamine of the general structure (VI) identified by  $\gamma$  and the end of Y identified 10 by  $\delta'$  is coupled to the atom of the thiazolamine of the general structure (VI) identified by  $\delta$ , with an aldehyde of the general structure (IV)



IV

wherein  $R^5$  is as defined above, and with an olefin of the 15 general structure (V)



V ,

- wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are as defined above, with the proviso that if one of the radicals R<sup>1</sup> and R<sup>2</sup> together with one of the radicals R<sup>3</sup> and R<sup>4</sup> form W, the end of W 5 identified by α' is joined to the α-carbon atom of the olefin of the general structure (V) and the end of W identified by β' is joined to the β-carbon atom of the olefin of the general structure (V), in the presence of an acid.

10

The processes according to the invention are preferably carried out in a "one-pot" reaction, in which a heterocyclamine of the general structure (II A), (II B) or (VI), an aldehyde of the general structure (IV) and an 15 olefin of the general structure (V) are simultaneously reacted with one another.

The acid that is used is an inorganic or organic protonic or Lewis acid. Preferably the reaction is carried out in 20 the presence of an organic acid, for example acetic acid, trifluoroacetic acid or methanesulfonic acid, especially trifluoroacetic acid.

The production process according to the invention may be 25 carried out in any suitable solvent in which the reactants are sufficiently soluble. Preferably organic solvents are used, for example dichloromethane or in particular acetonitrile.

The processes according to the invention are conveniently carried out at a temperature of 0° to 100°C, in particular 15° to 40°C. The reaction time is preferably 15 minutes to 12 hours and may be adapted to the respective requirements.

5

All heterocycllamines of the general structure (III) or (VI), the aldehydes of the general structure (IV) and the olefins of the general structure (V) that are used in the processes according to the invention are commercially

10 available (from Acros, Geel; Avocado, Port of Heysham; Aldrich, Delsenhofen; Fluka, Seelze; Lancaster, Mülheim; Maybridge, Tintagel; Merck, Darmstadt; Sigma, Deisenhofen; TCI, Japan) or may be prepared according to processes generally known in the prior art.

15

The processes according to the invention may also be carried out in semi-automated or fully automated form as parallel synthesis of a group of compounds of the general structure (I A), (I B) and/or (II) according to the 20 invention. Accordingly, substance libraries that contain at least one compound and preferably at least 48, in particular 96 and most particularly preferably 384 compounds of the general structure (I A), (I B) or (II) as defined above are also the subject of the present 25 invention.

For the purposes of the present invention the expression "substance library" is understood to denote a group of compounds that are prepared according to the same process 30 under identical or almost identical reaction conditions and by varying one reactant or several reactants. Such a substance library may contain the library items both as individual pure compounds as well as in the form of a

mixture of these compounds. With the aid of this substance library a medical screening for example may be performed in an automated manner in one or several *in vitro* screening processes.

5

The compounds of the general structure (I A) and/or (I B) or (II) may be isolated both as the substance *per se* as well as in the form of a salt. The substances of the general structure (I A), (I B) or (II) are usually obtained 10 by reaction according to the process outlined above followed by conventional working-up. The compounds that are thereby obtained may then be converted into the corresponding salt by for example adding an inorganic or organic acid, preferably hydrochloric acid, hydrobromic 15 acid, sulfuric acid, phosphoric acid, methanesulfonic acid, p-toluenesulfonic acid, carbonic acid, formic acid, acetic acid, oxalic acid, succinic acid, tartaric acid, mandelic acid, fumaric acid, lactic acid, citric acid, glutamic acid or aspartic acid. The salts that are formed include, *inter* 20 alia, hydrochlorides, hydrobromides, phosphates, carbonates, hydrogen carbonates, formates, acetates, oxalates, succinates, tartrates, fumarates, citrates and glutamates. In the case where the compounds of the general structure (I A), (I B) and/or (II) are acids, in particular 25 carboxylic acids (for example if  $R^5 = (CO_2H)$ , the salt formation may be carried out by addition of a base, for example sodium hydroxide,  $NaHCO_3$  or sodium carbonate; for the (carboxylic) acids it is particularly preferred to form the sodium salt. The particularly preferred hydrochloride 30 formation may in particular also be carried out by adding trimethylsilyl chloride (TMSC) to the base (I A), (I B) or (II) dissolved in a suitable organic solvent. The formation of sodium salts may be carried out by for example

titrating the compound (I A), (I B) or (II) dissolved in a suitable solvent, for example a water-methanol mixture, with sodium hydroxide solution.

5 Where the compounds of the general structure (I A), (I B) or (II) are obtained in the production process according to the invention as racemates or as mixtures of their various enantiomers and/or diastereomers, these mixtures may be separated according to processes that are well known in the  
10 prior art. Suitable methods include, *inter alia*, chromatographic separation processes, in particular liquid chromatography processes under normal or elevated pressure, preferably MPLC and HPLC processes, as well as fractional crystallisation processes. In this connection in  
15 particular individual enantiomers may be separated from one another for example by means of chiral phase HPLC or by means of crystallisation of diastereomer salts formed with chiral acids, for example (+)-tartaric acid, (-)-tartaric acid or (+)-10-camphorsulfonic acid or - where acids are  
20 involved - formed with chiral bases, for example brucine or (-)-ephedrine.

Moreover the present invention also provides a medicament that comprises at least one of the compounds according to  
25 the invention of the general structure (I a), (I B) or (II) as defined above and/or their pharmaceutically acceptable salts. In this connection the compounds according to the invention may be present in the medicament according to the invention as isomer-pure, in particular enantiomer-pure  
30 and/or diastereomer-pure compounds, but also as a racemic or non-racemic mixture. Preferably the medicament contains a pharmaceutically acceptable salt of the compounds

according to the invention, in particular a hydrochloride or a sodium salt.

The present invention also provides for the use of at least 5 one compound according to the invention of the general structure (I A), (I B) or (II), including their diastereomers or enantiomers, also as racemates or as an enantiomer mixture, in the form of their free base or acid or in the form of a salt formed with a physiological 10 compatible acid or base, in particular the hydrochloride salt and sodium salt, for the production of a medicament for pain relief. The compounds according to the invention have proved analgesically effective and bind to the MK801 binding site of the ionotropic NMDA receptor.

15

It has also been found as a result of binding to the MK801 binding site that the compounds according to the invention of the general structure (I A), (I B) or (II) are very suitable for treating further medical conditions, in 20 particular for treating epilepsy, schizophrenia, neurodegenerative conditions, in particular Alzheimer's disease, Huntington's disease and Parkinson's disease, cerebral ischaemias and infarcts, psychoses due to raised amino acid levels, cerebral oedemas, insufficiency states 25 of the central nervous system, in particular in hypoxia and anoxia, AIDS dementia, encephalomyelitis, Tourette's syndrome, perinatal asphyxia and tinnitus. The present application also provides for the use of at least one compound according to the invention of the general 30 structure (I A), (I B) or (II) including a pharmaceutically acceptable salt, for the production of a medicament for the treatment and/or prophylaxis of epilepsy, schizophrenia, neurodegenerative conditions, in particular Alzheimer's

disease, Huntington's disease and Parkinson's disease, cerebral ischaemias and infarcts, psychoses due to raised amino acid levels, cerebral oedemas, insufficiency states of the central nervous system, in particular in hypoxia and 5 anoxia, AIDS dementia, encephalomyelitis, Tourette's syndrome, perinatal asphyxia and/or tinnitus.

It has furthermore surprisingly been shown that the compounds according to the invention of the general formula 10 (I A) and/or (I B) are suitable ligands, in particular pharmacologically active ligands, of nucleoside transport proteins and/or of adenosine kinase and/or of adenosine deaminase and/or of A<sub>1</sub> and/or of A<sub>2</sub> and/or of A<sub>3</sub> receptors.

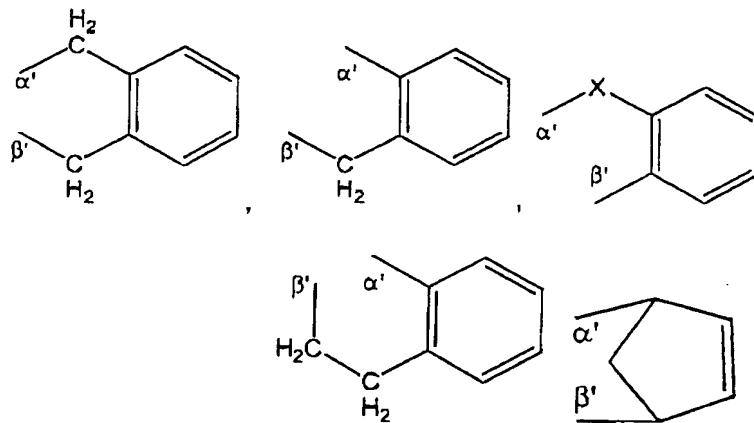
15 It is known that adenosine and ATP (adenosine-5'-triphosphate) and the purinergic receptors (purinoreceptors; P1 and P2 receptors) binding the latter play a significant role in the transmission and propagation of sensory information both in peripheral nerves as well as in the 20 dorsal horn (M.W. Salter, A. Sollevi, "Handbook of exp. pharmacol.", Chapter 13, (2001), pp. 371-401). In particular adenosine and ATP as well as the P1 and P2 receptors play a role in the development and propagation of pain. With the P1 and P2 receptors a distinction is made 25 between the so-called ATP receptors (= P2 receptors) and the so-called adenosine receptors (= P1 receptors). Among these P1 receptors four sub-types have been identified up to the present time, namely A<sub>1</sub>, A<sub>2a</sub>, A<sub>2b</sub> and A<sub>3</sub>, all of which belong to the family of G protein-coupled receptors (GPCR). 30 (Hereinafter the two sub-types A<sub>2a</sub> and A<sub>2b</sub> will also be identified as A<sub>2</sub> sub-type.)

Other substances that also have an influence on the adenosine level in the body are adenosine kinase, which catalyses the conversion of adenosine into AMP (adenosine-5'-monophosphate), adenosine deaminase, which catalyses the 5 hydrolytic deamination of adenosine and 2'-deoxyadenosine to, respectively, inosine and 2'-deoxyinosine, and the nucleoside transport proteins, which are involved in the transport of, *inter alia*, adenosine from the extracellular space into the cell and vice versa. The latter play a role 10 in particular in neuropathic pain states.

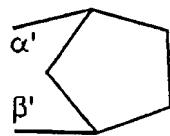
On account of the properties that have now been discovered, the present invention also provides for the use of compounds of the general formula (I A) or (I B) in the form 15 shown above or in the form of their acid(s) or their base(s) or in the form of one of their salts, in particular one of the physiologically compatible salts, or in the form of one of their solvates, in particular the hydrates; in the form of their racemate; in the form of the pure 20 stereoisomers, in particular enantiomers or diastereomers, or in the form of mixtures of the stereoisomers, in particular of the enantiomers or diastereomers, in an arbitrary mixture ratio; in which R<sup>1</sup> and R<sup>2</sup> independently of one another denote H, O-R<sup>9</sup>, S-R<sup>10</sup>, 25 C<sub>1-12</sub>-alkyl, C<sub>3-8</sub>-cycloalkyl, -CH<sub>2</sub>-C<sub>3-8</sub>-cycloalkyl, aryl, -(C<sub>1-6</sub>-alkyl)-aryl, heterocyclyl or -(C<sub>1-6</sub> alkyl)-heterocyclyl, in which one of the radicals R<sup>1</sup> and R<sup>2</sup> is H and the other radical of R<sup>1</sup> and R<sup>2</sup> is not H, or in the 30 case that one of the radicals R<sup>1</sup> and R<sup>2</sup> denotes aryl, the other radical of R<sup>1</sup> and R<sup>2</sup> denotes H or C<sub>1-12</sub>-alkyl,

$R^3$  and  $R^4$  denote H,  $C_{1-12}$ -alkyl,  $C_{3-8}$ -cycloalkyl,  $-CH_2-C_{3-8}-$  cycloalkyl, aryl or  $-(C_{1-6}$ -alkyl)-aryl  
in which at least one of the radicals  $R^3$  and  $R^4$  is H, or

- 5 one of the radicals  $R^1$  and  $R^2$  together with one of the radicals  $R^3$  and  $R^4$  forms W,  
where W denotes  $\alpha'-(CH_2)_n-\beta'$  where  $n = 3, 4, 5$  or 6,  $\alpha'-CH=CH-CH_2-\beta'$ ,  $\alpha'-CH_2-CH=CH-\beta'$ ,  $\alpha'-CH=CH-CH_2-CH_2-\beta'$ ,  $\alpha'-CH_2-CH=CH-CH_2-\beta'$ ,  $\alpha'-CH_2-CH_2-CH_2-CH=CH-\beta'$ ,  $\alpha'-O-(CH_2)_m-\beta'$   
10 where  $m = 2, 3, 4$  or 5,



where  $X = CH_2, O$  or  $S$ ,



, the end of W identified by  $\alpha'$  is joined to the atom of the compound of the general formula (I A) and/or (I B) identified by  $\alpha$ , and the end of W identified by  $\beta'$  is joined to the atom of the compound of the general structure (I A) and/or (I B) identified by  $\beta$ , the other radical of  $R^1$  and  $R^2$  is H or  $C_{1-12}$ -alkyl, and the other radical of  $R^3$  and  $R^4$  is H or  $C_{1-12}$ -alkyl;

- 15  
20  $R^5$  denotes  $C_{1-12}$ -alkyl,  $C_{3-8}$ -cycloalkyl,  $-CH_2-C_{3-8}-$  cycloalkyl, aryl,  $-(C_{1-6}$  alkyl)-aryl,

heterocyclyl, - (C<sub>1-6</sub> alkyl) -heterocyclyl or  
 C(=O)R<sup>11</sup>;  
 R<sup>6</sup> denotes H, C<sub>1-8</sub>-alkyl, -CN, fluorine, chlorine,  
 bromine, iodine, NO<sub>2</sub>, NH<sub>2</sub>, NHR<sup>12</sup>, NR<sup>13</sup>R<sup>14</sup>, OR<sup>15</sup>,  
 5 S(O)<sub>p</sub>R<sup>16</sup> where p = 0, 1 or 2, -C(=O)R<sup>17</sup> or  
 -N=N-aryl;  
 R<sup>7</sup> denotes H, C<sub>1-8</sub>-alkyl, aryl, -CN, fluorine,  
 chlorine, bromine, iodine, NO<sub>2</sub>, NH<sub>2</sub>, NHR<sup>12</sup>, NR<sup>13</sup>R<sup>14</sup>,  
 OR<sup>18</sup>, S(O)<sub>q</sub>R<sup>19</sup> where q = 0, 1 or 2 or denotes  
 10 C(=O)R<sup>20</sup>;  
 R<sup>9</sup> and R<sup>10</sup> independently of one another denote H, C<sub>1-8</sub>-alkyl,  
 C<sub>3-8</sub>-cycloalkyl, -CH<sub>2</sub>-C<sub>3-8</sub>-cycloalkyl, aryl or  
 - (C<sub>1-6</sub>-alkyl) -aryl;  
 R<sup>11</sup> denotes H, C<sub>1-8</sub>-alkyl, C<sub>3-8</sub>-cycloalkyl, -CH<sub>2</sub>-C<sub>3-8</sub>-  
 15 cycloalkyl, aryl or OR<sup>25</sup>;  
 R<sup>12</sup> denotes C<sub>1-6</sub>-alkyl or -CH<sub>2</sub>-aryl;  
 R<sup>13</sup> and R<sup>14</sup> are identical or different C<sub>1-6</sub>-alkyl or together  
 denote -(CH<sub>2</sub>)<sub>h</sub>- where h = 4 or 5;  
 R<sup>15</sup> and R<sup>16</sup> independently of one another denote H, C<sub>1-8</sub>-alkyl,  
 20 C<sub>3-8</sub>-cycloalkyl, -CH<sub>2</sub>-C<sub>3-8</sub>-cycloalkyl, aryl or  
 - (C<sub>1-6</sub>-alkyl) -aryl;  
 R<sup>17</sup> denotes H, C<sub>1-8</sub>-alkyl, C<sub>3-8</sub>-cycloalkyl, -CH<sub>2</sub>-C<sub>3-8</sub>-  
 cycloalkyl, aryl, - (C<sub>1-6</sub>-alkyl) -aryl, NH<sub>2</sub>, NHR<sup>12</sup>,  
 NR<sup>13</sup>R<sup>14</sup> or OR<sup>26</sup>;  
 25 R<sup>18</sup> and R<sup>19</sup> independently of one another denote H, C<sub>1-8</sub>-alkyl,  
 C<sub>3-8</sub>-cycloalkyl, -CH<sub>2</sub>-C<sub>3-8</sub>-cycloalkyl, aryl or  
 - (C<sub>1-6</sub>-alkyl) -aryl;  
 R<sup>20</sup> denotes H, C<sub>1-8</sub>-alkyl, C<sub>3-8</sub>-cycloalkyl, -CH<sub>2</sub>-C<sub>3-8</sub>-  
 cycloalkyl, aryl or - (C<sub>1-6</sub>-alkyl) -aryl or OR<sup>27</sup>;  
 30 R<sup>25</sup>, R<sup>26</sup>, and R<sup>27</sup> independently of one another denote H or  
 C<sub>1-6</sub>-alkyl, where R<sup>25</sup> does not denote H if  
 simultaneously R<sup>1</sup> denotes aryl and R<sup>2</sup> denotes  
 alkyl;

for the prevention and/or treatment and for the production of a medicament for the prevention and/or treatment of medical conditions and/or illnesses that are influenced via a modulation, i.e., stimulation and/or inhibition, of 5 nucleoside transport proteins and/or of adenosine kinase and/or of adenosine deaminase and/or of A<sub>1</sub> and/or of A<sub>2</sub> and/or of A<sub>3</sub> receptors.

Preferably the compounds of the general formula (1A) and/or (1B) are therefore used for the prevention and/or treatment of and for the production of a medicament for the prevention and/or treatment of pain, neuropathic pain, respiratory pathway conditions, cancer, cardiac arrhythmias, ischaemias, epilepsy, Huntington's disease, malfunctions 15 and diseases of the immune system, inflammatory conditions and diseases, neonatal hypoxia, neurodegenerative conditions, Parkinson's disease, kidney failure, schizophrenia, sleep disturbances, strokes, thromboses, urinary incontinence, diabetes, psoriasis, septic shock, 20 cerebral trauma, glaucoma and/or congestive insufficiency. The compounds of the general formulae (I A) and/or (I B) have proved effective in treating these conditions. In addition side effects that normally occur when using conventional opioid analgesics are not or are only rarely 25 observed with these compounds.

In addition the present invention also provides pharmaceutical compositions that contain at least one compound of the general structure (I A), (I B) or (II) 30 defined above or one of their pharmaceutically acceptable salts and one or more pharmaceutical auxiliary substances.

The medicaments and pharmaceutical compositions according to the invention may exist and be administered as liquid, semi-solid or solid medicament forms and in the form of for example injectable solutions, drops, juices, syrups, sprays, suspensions, granules, tablets, pellets, transdermal therapeutic systems, capsules, plasters, suppositories, ointments, creams, lotions, gels, emulsions or aerosols and, depending on the pharmaceutical form, contain in addition to at least one compound according to 10 the invention of the general structure(I A), (I B) or (II), also pharmaceutical auxiliary substances such as for example carrier materials, fillers, solvents, diluents, surfactants, colourants, preservatives, release agents, intestinal lubricants, lubricants, aroma substances and/or 15 binders. These auxiliary substances may for example be water, ethanol, 2-propanol, glycerol, ethylene glycol, propylene glycol, polyethylene glycol, polypropylene glycol, glucose, fructose, lactose, sucrose, dextrose, molasses, starch, modified starch, gelatin, sorbitol, 20 inositol, mannitol, microcrystalline cellulose, methylcellulose, carboxymethylcellulose, cellulose acetate, shellac, cetyl alcohol, polyvinylpyrrolidone, paraffins, waxes, natural and synthetic gums, gum arabic, alginates, dextran, saturated and unsaturated fatty acids, stearic 25 acid, magnesium stearate, zinc stearate, glyceryl stearate, sodium lauryl sulfate, edible oils, sesame oil, coconut oil, groundnut oil, soya bean oil, lecithin, sodium lactate, polyoxyethylene and polyoxypropylene fatty acid esters, sorbitan fatty acid esters, sorbic acid, benzoic acid, citric acid, ascorbic acid, tannic acid, sodium 30 chloride, potassium chloride, magnesium chloride, calcium chloride, magnesium oxide, zinc oxide, silicon dioxide, titanium oxide, titanium dioxide, magnesium sulfate, zinc

sulfate, calcium sulfate, potassium carbonate, calcium phosphate, dicalcium phosphate, potassium bromide, potassium iodide, talcum, kaolin, pectin, crospovidone, agar and bentonite.

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The choice of the auxiliary substances as well as the amounts thereof to be employed depends on whether the medicament is to be administered orally, subcutaneously, parenterally, intravenously, vaginally, pulmonarily, 10 intraperitoneally, transdermally, intramuscularly, nasally, buccally, rectally or topically, for example to treat infections of the skin, mucous membranes and eyes. For oral administration, *inter alia* preparations in the form of tablets, sugar-coated pills, capsules, granules, drops, 15 juices and syrups are suitable, while for parenteral, topical and inhalative application solutions, suspensions, readily reconstitutable powders for inhalation as well as sprays are suitable. Compounds according to the invention of the general structure (I A), (I B) or (II) in a dépôt in 20 dissolved form or in a plaster, optionally with the addition of agents promoting skin penetration, are suitable percutaneous application preparations. Preparation forms that may be used for rectal, transmucosal, parenteral and/or percutaneous administration may provide for the 25 delayed release of the compounds according to the invention of the general structure (I A), (I B) or (II).

The production of the medicaments and pharmaceutical compositions according to the invention is carried out with 30 the aid of agents, devices, methods and processes well known in the prior art relating to pharmaceutical formulations, such as are described for example in "Remington's Pharmaceutical Sciences", Ed. A.R. Gennaro,

17<sup>th</sup> Edition, Mack Publishing Company, Easton, Pa. (1985), in particular in Part 8, Chapters 76 to 93.

Thus for example for a solid formulation such as a tablet, 5 the active constituent of the medicament, i.e. a compound of the general structure (I A), (I B) or (II) or one of its pharmaceutically acceptable salts, may be granulated with a pharmaceutical carrier, for example customary tablet constituents such as maize starch, lactose, sucrose, 10 sorbitol, talcum, magnesium stearate, dicalcium phosphate or pharmaceutically acceptable gums, and pharmaceutical diluents, such as for example water, in order to form a solid composition that contains a compound according to the invention or a pharmaceutically acceptable salt thereof in 15 a state of homogeneous distribution. The expression "homogeneous distribution" is understood in the present context to mean that the active substance is distributed uniformly throughout the whole composition so that the latter can be directly subdivided into equally effective 20 unit-dose forms such as tablets, pills or capsules. The solid composition is then subdivided into unit-dose forms. The tablets or pills of the medicament according to the invention and/or of the compositions according to the invention may also be coated or otherwise compounded in 25 order to provide a delayed-release dose form. Suitable coating agents include, *inter alia*, polymeric acids and mixtures of polymeric acids with materials such as for example shellac, cetyl alcohol and/or cellulose acetate.

30 The amount of active substance to be administered to the patient varies and depends on the patient's weight, age and medical history, as well as on the type of application, medical indications and severity of the condition.

Normally 0.1 to 5000 mg/kg, in particular 1 to 500 mg/kg and preferably 2 to 250 mg/kg bodyweight of at least one compound according to the invention of the general structure (I A), (I B) or (II) are administered.

5

The following examples serve to describe the present invention in more detail:

**Examples**

The chemicals and solvents that were used were obtained commercially from one of the following suppliers: Acros, Geel; Avocado, Port of Heysham; Aldrich, Deisenhofen; 5 Fluka, Seelze; Lancaster, Mülheim; Maybridge, Tintagel; Merck, Darmstadt; Sigma, Deisenhofen; TCI, Japan; or are prepared according to processes generally known in the prior art.

10 General operating protocol (semi-automated synthesis)

A threaded round-bottom glass tube (diameter 16 mm, length 125 mm) was fitted with a stirrer and sealed with a screw cap provided with a septum. The tube was placed in a 15 stirring block adjusted to a temperature of 20°C. The following reagents were then successively pipetted in:

1. 1 ml of a solution containing 0.1 M trifluoroacetic acid and 0.1 M heterocyclamine component (III) or (VI), in acetonitrile
- 20 2. 1 ml of a 0.11 M aldehyde (IV) solution in acetonitrile
3. 1 ml of a 0.3 M olefin (V) solution in acetonitrile

The reaction mixture was stirred for 600 minutes at 20°C in 25 one of the stirring blocks. The reaction solution was then filtered off at the filtration station. The test tube was rinsed twice with 1.5 ml of a 7.5% NaHCO<sub>3</sub> solution. The rack together with the samples was placed manually on the working-up unit. 2 ml of diethyl ether were added to the 30 reaction mixture in a Vortexer and shaken. The mixture was briefly centrifuged to form a phase boundary. The phase boundary was optically detected and the organic phase was pipetted off.

In the next step 2 ml of diethyl ether were again added to the aqueous phase, the whole was shaken and centrifuged, and the organic phase was pipetted off. The combined 5 organic phases were dried over 2.4 g of granulated MgSO<sub>4</sub>. The solvent was removed in a vacuum centrifuge.

Each sample was analysed by means of ESI-MS and/or NMR. Mass spectroscopy investigations (ESI-MS) were carried out 10 with an LCQ Classic mass spectrometer from the Finnegan company. <sup>1</sup>H-NMR investigations of the compounds according to the invention were carried out with a 300 MHz DPX Advance NMR apparatus from Bruker.

15 The example compounds 1-144, 146-151 as well as 153 and 154 were prepared according to the aforescribed general operating protocol (see Table 1).

Table 1

Exmp.	Name	Calculated Mol. Wt.	Found Mol. Wt.
1	3-bromo-5-(5-nitrofuran-2-yl)-7-m-tolyltetrahydropyrazolo[1,5-a]pyrimidine	403.24	403.2/405.1
2	3-bromo-7-(4-fluorophenyl)-7-methyl-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine	421.23	421.1/423.0
3	3-bromo-7-naphthalin-2-yl-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine	439.27	439.2/441.1
4	2-(3-bromo-7-m-tolyltetrahydropyrazolo[1,5-a]pyrimidin-5-yl)-cyclopropanecarboxylic acid ethyl ester	404.31	404.5/406.4
5	2-[3-bromo-7-(4-bromophenyl)-tetrahydropyrazolo[1,5-a]pyrimidin-5-yl]-cyclopropanecarboxylic acid ethyl ester	469.18	468.3/470.1 /472.1
6	2-(3-bromo-7-naphthalin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidin-5-yl)-cyclopropanecarboxylic acid ethyl ester	440.34	440.5/442.5
7	3-bromo-7-(4-fluorophenyl)-7-methyl-5-(5-methylfuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine	390.26	390.1/392.0
8	3-bromo-7-(3,4-dimethoxyphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-5-carboxylic acid ethyl ester	410.27	410.3/412.2
9	3-bromo-7-(4-methoxyphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-5-carboxylic acid ethyl ester	380.24	380.2/382.1
10	3-bromo-7-(4-methoxyphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-5-carboxylic acid	352.19	354.2
11	3-bromo-7-(2,4-dimethylphenyl)-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine	417.26	417.1/419.0
12	3-bromo-7-(4-methoxyphenyl)-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine	419.23	419.0/421.0
13	5,5a,6,8a-tetrahydro-3H-1,4,8b-triaza-as-indacene-3,5-dicarboxylic acid diethyl ester; 5,5a,6,8a-tetrahydro-4H-1,4,8b-triaza-as-indacene-3,5-dicarboxylic acid diethyl ester	305.33	306.1
14	2-hydroxy-3-phenylazo-5,5a,6,8a-tetrahydro-3H-1,4,8b-triaza-as-indacene-5-carboxylic acid ethyl ester; 2-hydroxy-3-phenylazo-5,5a,6,8a-tetrahydro-4H-1,4,8b-	353.38	354.3

Exmp.	Name	Calculated Mol. Wt.	Found Mol. Wt.
	triaza-as-indacene-5-carboxylic acid ethyl ester		
15	2-tert.-butyl-5,5a,6,8a-tetrahydro-3H-1,4,8b-triaza-as-indacene-5-carboxylic acid ethyl ester; 2-tert.-butyl-5,5a,6,8a-tetrahydro-3H-1,4,8b-triaza-as-indacene-5-carboxylic acid ethyl ester	289.37	290.3
16	3-bromo-2-phenyl-5,5a,6,8a-tetrahydro-3H-1,4,8b-triaza-as-indacene-5-carboxylic acid ethyl ester; 3-bromo-2-phenyl-5,5a,6,8a-tetrahydro-4H-1,4,8b-triaza-as-indacene-5-carboxylic acid ethyl ester	388.26	388.2/390.1
17	7-(2,3,4-trimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-3,5-dicarboxylic acid diethyl ester	433.46	434.4
18	3-cyano-2-methylsulfanyl-7-(2,3,4-trimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester	432.49	433.2
19	2-hydroxy-7-(4-hydroxyphenyl)-6-methyl-3-phenylazo-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester	421.45	422.4
20	3-bromo-7-(4-hydroxyphenyl)-6-methyl-2-phenyltetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester	456.34	456.4/458.4
21	5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-3,5-dicarboxylic acid diethyl ester; 5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluorene-3,5-dicarboxylic acid diethyl ester	355.39	356.2
22	2-hydroxy-3-phenylazo-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-5-carboxylic acid ethyl ester; 2-hydroxy-3-phenylazo-5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluorene-5-carboxylic acid ethyl ester	403.44	404.3
23	7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3,5-dicarboxylic acid diethyl ester	375.44	376.2
24	3-cyano-2-methylsulfanyl-7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester	374.48	375.1
25	3-cyano-2-methylsulfanyl-7-(2,3,4-trimethoxyphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid	404.44	405.2
26	7-phenylsulfanyltetrahydropyrazolo-	347.39	348.2

Exmp.	Name	Calculated Mol. Wt.	Found Mol. Wt.
	[1,5-a]pyrimidine-3,5-dicarboxylic acid-3-ethyl ester		
27	3-cyano-7-(2,4-dimethylphenyl)-2-methylsulfanyl-tetrahydropyrazolo-[1,5-a]pyrimidine-5-carboxylic acid ethyl ester	370.47	371.2
28	3-cyano-7-(2,4-dimethylphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-5-carboxylic acid ethyl ester	324.38	325.2
29	7-(2,4-dimethylphenyl)-tetrahydro-pyrazolo[1,5-a]pyrimidine-3,5-dicarboxylic acid-3-ethyl ester	343.38	344.2
30	3-bromo-7-(2,4-dimethylphenyl)-2-phenyltetrahydropyrazolo-[1,5-a]-pyrimidine-5-carboxylic acid	426.31	426.2/428.1
31	3-cyano-7-(2,4-dimethylphenyl)-2-methylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid	342.42	343.2
32	3-cyano-7-(2,4-dimethylphenyl)-tetrahydropyrazolo-[1,5-a]pyrimidine-5-carboxylic acid	296.32	297.2
33	3-cyano-7-(3,4-dimethoxyphenyl)-2-methylsulfanyl-tetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid	374.41	376.2
34	7-(2,4-dimethylphenyl)-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo-[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	410.42	411.1
35	7-(2,4-dimethylphenyl)-5-(5-nitrofuran-2-yl)-3-phenylazotetrahydropyrazolo[1,5-a]pyrimidin-2-ol	458.47	459.3
36	3-bromo-7-(2,4-dimethylphenyl)-5-(5-nitrofuran-2-yl)-2-phenylazo-tetrahydropyrazolo[1,5-a]pyrimidine	493.36	493.2/495.1
37	7-(2,4-dimethylphenyl)-2-methylsulfanyl-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carbonitrile	409.46	410.1
38	7-(2,4-dimethylphenyl)-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	363.37	364.1
39	3-bromo-7-(3,4-dimethoxyphenyl)-5-(5-nitrofuran-2-yl)-2-phenyl-tetrahydropyrazolo[1,5-a]pyrimidine	525.36	525.4/527.1
40	7-(4-methoxyphenyl)-2-methylsulfanyl-5-(5-nitrofuran-2-yl)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carbonitrile	411.43	412.9
41	7-(2,4-dimethylphenyl)-5-(2-ethoxycarbonylcyclo-propyl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid	411.5	412.5

Exmp.	Name	Calculated Mol. Wt.	Found Mol. Wt.
	ethyl ester		
42	2-[7-(2,4-dimethylphenyl)-2-hydroxy-3-phenylazotetrahydropyrazolo[1,5-a]pyrimidin-5-yl]-cyclopropanecarboxylic acid ethyl ester	459.54	460.3
43	2-[2-tert.-butyl-7-(2,4-dimethylphenyl)tetrahydropyrazolo[1,5-a]pyrimidin-5-yl]cyclopropane-carboxylic acid ethyl ester	395.54	396.5
44	2-[3-bromo-7-(2,4-dimethylphenyl)-2-phenyltetrahydropyrazolo[1,5-a]pyrimidin-5-yl]cyclopropane-carboxylic acid ethyl ester	494.43	494.4/496.2
45	2-[3-cyano-7-(2,4-dimethylphenyl)-2-methylsulfanyl]tetrahydropyrazolo[1,5-a]pyrimidin-5-yl]cyclopropane-carboxylic acid ethyl ester	410.53	411.3
46	5-(2-ethoxycarbonylcyclopropyl)-7-(3-fluorophenyl)tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	401.43	402.2
47	2-[3-bromo-7-(3-bromophenyl)-2-phenyltetrahydropyrazolo[1,5-a]pyrimidin-5-yl]cyclopropane-carboxylic acid ethyl ester	545.28	544.3/546.1 / 548.0
48	2-[7-(3-bromophenyl)-3-cyano-2-methylsulfanyl]tetrahydropyrazolo[1,5-a]pyrimidin-5-yl]cyclopropane-carboxylic acid ethyl ester	461.38	461.2/463.0
49	7-(2,4-dimethylphenyl)-5-(5-nitrothiophen-2-yl)-3-phenylazotetrahydropyrazolo[1,5-a]pyrimidin-2-ol	474.54	475.2
50	7-(2,4-dimethylphenyl)-2-methylsulfanyl-5-(5-nitrothiophen-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	425.53	426.1
51	7-(2,4-dimethylphenyl)-5-(5-nitrothiophen-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	379.44	380.1
52	7-(3,4-dimethoxyphenyl)-5-(5-nitrothiophen-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	458.49	459.3
53	7-(3,4-dimethoxyphenyl)-5-(5-nitrothiophen-2-yl)-3-phenylazotetrahydropyrazolo[1,5-a]pyrimidin-2-ol	506.54	507.2
54	3-bromo-7-(3,4-dimethoxyphenyl)-5-(5-nitrothiophen-2-yl)-2-phenyltetrahydropyrazolo[1,5-a]pyrimidine	541.42	541.4/543.3
55	7-(3,4-dimethoxyphenyl)-2-methylsulfanyl-5-(5-nitrothiophen-2-yl)-	457.53	458.1

Exmp.	Name	Calculated Mol. Wt.	Found Mol. Wt.
	tetrahydropyrazolo[1,5-a]-pyrimidine-3-carbonitrile		
56	7-(3,4-dimethoxyphenyl)-5-(5-nitrothiophen-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	411.43	412.1
57	7-(4-methoxyphenyl)-5-(5-nitrothiophen-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	428.46	429.1
58	5-[3-bromo-7-(4-methoxyphenyl)-2-phenyltetrahydropyrazolo[1,5-a]-pyrimidin-5-yl]-furan-2-carboxylic acid	494.34	494.2/496.1
59	5-benzoyl-7-(2,4-dimethylphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carboxylic acid ethyl ester	403.48	404.2
60	5-benzoyl-7-(2,4-dimethylphenyl)-2-methylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	402.51	403.1
61	5-benzoyl-7-(2,4-dimethylphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carbonitrile	356.42	355.3/357.2
62	5-benzoyl-7-(3,4-dimethoxyphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carboxylic acid ethyl ester	435.47	436.2
63	[3-bromo-7-(3,4-dimethoxyphenyl)-2-phenyltetrahydro-pyrazolo[1,5-a]-pyrimidin-5-yl]phenylmethanone	518.41	518.7/520.2
64	5-benzoyl-7-(3,4-dimethoxyphenyl)-2-methylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	434.51	435.1
65	5-benzoyl-7-(3,4-dimethoxyphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carbonitrile	388.42	389.1
66	5-benzoyl-7-(4-methoxyphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carboxylic acid ethyl ester	405.45	406.1
67	5-benzoyl-7-(4-methoxyphenyl)-2-methylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	404.49	405.0
68	5-benzoyl-7-(4-methoxyphenyl)tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	358.4	359.0
69	5-benzoyl-7-(3-fluorophenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carboxylic acid ethyl ester	393.41	394.4
70	[3-bromo-7-(3-fluorophenyl)-2-phenyltetrahydropyrazolo[1,5-a]-pyrimidin-5-yl]-phenylmethanone	476.35	476.3/478.3

Exmp.	Name	Calculated Mol. Wt.	Found Mol. Wt.
71	[3-bromo-7-(3-bromophenyl)-2-phenyltetrahydro-pyrazolo[1,5-a]-pyrimidin-5-yl]phenylmethanone	537.26	538.4
72	7-(2,4-dimethylphenyl)-5-(4-phenoxyphenyl)tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	467.56	468.2
73	3-bromo-7-(2,4-dimethylphenyl)-5-(4-phenoxyphenyl)-2-phenyltetrahydro-pyrazolo[1,5-a]pyrimidine	550.5	550.3/552.2
74	7-(2,4-dimethylphenyl)-2-methylsulfanyl-5-(4-phenoxyphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carbonitrile	466.6	467.1
75	7-(2,4-dimethylphenyl)-5-(4-phenoxyphenyl)tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	420.51	421.1
76	7-(3,4-dimethoxyphenyl)-5-(4-phenoxyphenyl)tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	499.56	500.2
77	7-(3,4-dimethoxyphenyl)-2-methylsulfanyl-5-(4-phenoxyphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carbonitrile	498.6	499.1
78	3-[3-cyano-7-(4-hydroxyphenyl)-6-methyltetrahydropyrazolo[1,5-a]-pyrimidin-5-yl]-2-hydroxybenzoic acid	390.39	391.1
79	3-(3-cyano-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]-fluoren-5-yl)-2-hydroxybenzoic acid; 3-(3-cyano-5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluoren-5-yl)-2-hydroxybenzoic acid	372.38	373.0
80	3-(3-cyano-7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidin-5-yl)-2-hydroxybenzoic acid	392.43	392.9
81	3-[2-tert.-butyl-7-(4-chlorophenyl)-7-methyltetrahydropyrazolo[1,5-a]pyrimidin-5-yl]-2-hydroxybenzoic acid	439.94	440.2
82	5-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)-6-methyltetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	423.46	424.1
83	5-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)-6-methyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	376.41	377.1
84	5-(4-hydroxy-3-methoxyphenyl)-5,5a,6,10b-tetrahydro-3H-1,4,10c-	405.45	406.0

Exmp.	Name	Calculated Mol. Wt.	Found Mol. Wt.
	triazacyclopenta[c]fluorene-3-carboxylic acid ethyl ester; 5-(4-hydroxy-3-methoxyphenyl)-5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluorene-3-carboxylic acid ethyl ester		
85	4-(2-tert.-butyl-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluoren-5-yl)-2-methoxyphenol; 4-(2-tert.-butyl-5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluoren-5-yl)-2-methoxyphenol	389.49	390.2
86	5-(4-hydroxy-3-methoxyphenyl)-2-methylsulfanyl-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-3-carbonitrile; 5-(4-hydroxy-3-methoxyphenyl)-2-methylsulfanyl-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-3-carbonitrile	404.49	404.9
87	5-(4-hydroxy-3-methoxyphenyl)-7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	425.5	426.0
88	4-(2-tert.-butyl-7-phenylsulfanyl-tetrahydro-pyrazolo[1,5-a]-pyrimidin-5-yl)-2-methoxyphenol	409.55	410.1
89	4-(3-bromo-2-phenyl-7-phenylsulfanyl-tetrahydro-pyrazolo[1,5-a]pyrimidin-5-yl)-2-methoxyphenol	508.44	508.2/510.0
90	5-(2-hydroxy-3-methoxyphenyl)-7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	425.5	425.0
91	7-(4-chlorophenyl)-5-(2-hydroxy-3-methoxyphenyl)-7-methyltetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	441.91	441.0
92	5-(4-hydroxybutyl)-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-3-carbonitrile; 5-(4-hydroxybutyl)-5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]fluorene-3-carbonitrile	308.38	309.3
93	5-(4-hydroxybutyl)-2-methylsulfanyl-7-phenyl-sulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	374.52	375.2
94	5-(4-hydroxybutyl)-7-phenylsulfanyltetrahydro-pyrazolo[1,5-a]pyrimidine-3-carbonitrile	328.43	329.2
95	7-(4-chlorophenyl)-5-(4-	344.84	345.1

Exmp.	Name	Calculated Mol. Wt.	Found Mol. Wt.
	hydroxybutyl)-7-methyltetrahydro-pyrazolo[1,5-a]pyrimidine-3-carbonitrile		
96	5-butyl-2-methylsulfanyl-5,5a,6,10b-tetrahydro-3H-1,4,10c-triazacyclopenta[c]fluorene-3-carbonitrile; 5-butyl-2-methylsulfanyl-5,5a,6,10b-tetrahydro-4H-1,4,10c-triazacyclopenta[c]-fluorene-3-carbonitrile	338.47	339.3
97	5-butyl-2-methylsulfanyl-7-phenylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	358.52	359.2
98	5-butyl-7-phenylsulfanyltetrahydro-pyrazolo[1,5-a]pyrimidine-3-carbonitrile	312.43	313.1
99	5-butyl-7-(4-chlorophenyl)-7-methylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	374.93	375.3
100	5-cyclopropyl-7-(2,4-dimethylphenyl)-3-phenylazotetrahydropyrazolo[1,5-a]pyrimidin-2-ol	387.48	388.5
101	2-tert.-butyl-5-cyclopropyl-7-(2,4-dimethylphenyl)-tetrahydropyrazolo[1,5-a]pyrimidine	323.48	324.6
102	5-cyclopropyl-7-(2,4-dimethylphenyl)-2-methylsulfanyltetrahydropyrazolo[1,5-a]-pyrimidine-3-carbonitrile	338.47	339.8
103	2-tert.-butyl-5-cyclopropyl-7-(3,4-dimethoxyphenyl)tetrahydropyrazolo[1,5-a]pyrimidine	355.48	356.3/357.6
104	3-bromo-5-cyclopropyl-7-(3,4-dimethoxyphenyl)-2-phenyltetrahydropyrazolo[1,5-a]pyrimidine	454.37	454.3/456.1
105	5-cyclopropyl-7-(4-methoxyphenol)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carboxylic acid ethyl ester	341.41	342.7
106	5-cyclopropyl-3,5,5a,6,7,11b-hexahydro-1,4,11c-triazacyclopenta[c]phenanthrene-3-carbonitrile	290.36	291.4
107	7-(2,4-dimethylphenyl)-5-pyridin-2-yl-tetrahydro-pyrazolo[1,5-a]-pyrimidine-3-carboxylic acid ethyl ester	376.45	377.3/378.4
108	7-(2,4-dimethylphenyl)-3-phenylazo-5-pyridin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidin-2-ol	424.5	425.3
109	3-bromo-7-(2,4-dimethylphenyl)-2-phenyl-5-pyridin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidine	459.39	459.7/462.2
110	7-(2,4-dimethylphenyl)-2-methylsulfanyl-5-pyridin-2-yl-tetrahydro-	375.49	376.4

Exmp.	Name	Calculated Mol. Wt.	Found Mol. Wt.
	pyrazolo[1,5-a]pyrimidine-3-carbonitrile		
111	7-(3,4-dimethoxyphenyl)-2-methylsulfanyl-5-phenethyl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	434.56	435.3
112	7-(3,4-dimethoxyphenyl)-5-phenethyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	388.47	389.2
113	5-cyclopropyl-7-(2-hydroxyethoxy)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	295.33	296.2
114	2-(2-tert.-butyl-5-cyclopropyl-tetrahydropyrazolo-[1,5-a]-pyrimidin-7-yloxy)-ethanol	279.38	280.3
115	5-cyclopropyl-3,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacene-3-carboxylic acid ethyl ester; 5-cyclopropyl-4,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacene-3-carboxylic acid ethyl ester	277.32	278.3
116	5-cyclopropyl-3-phenylazo-3,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacen-2-ol; 5-cyclopropyl-3-phenylazo-4,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacen-2-ol	325.37	326.5
117	7-cyclohexyloxy-5-cyclopropyltetrahydropyrazolo[1,5-a]pyrimidin-3-carboxylic acid ethyl ester	333.43	334.1
118	7-cyclohexyloxy-5-cyclopropyl-2-methylsulfanyltetrahydropyrazolo-[1,5-a]pyrimidin-3-carbonitrile	332.46	333.2
119	7-(4-chlorophenyl)-5-cyclohexyl-tetrahydropyrazolo[1,5-a]pyrimidin-3-carbonitrile	340.85	341.4
120	5-cyclohexyl-7-(2-hydroxyethoxy)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carboxylic acid ethyl ester	337.41	338.3
121	5-cyclohexyl-3,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacene-3-carboxylic acid ethyl ester; 5-cyclohexyl-4,5,5a,6,7,8a-hexahydro-8-oxa-1,4,8b-triaza-as-indacene-3-carboxylic acid ethyl ester	319.4	320.3
122	5-cyclohexyl-7-cyclohexyloxy-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carboxylic acid ethyl ester	375.51	376.2
123	7-(2,4-dimethylphenyl)-3-phenylazo-	389.5	390.5

Exmp.	Name	Calculated Mol. Wt.	Found Mol. Wt.
	5-propyl-tetrahydropyrazolo[1,5-a]-pyrimidin-2-ol		
124	7-(2,4-dimethylphenyl)-2-methylsulfanyl-5-propyltetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	340.49	341.3
125	5-tert.-butyl-7-(2,4-dimethylphenyl)-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carboxylic acid ethyl ester	355.48	356.1
126	2,5-di-tert.-butyl-7-(3,4-dimethoxyphenyl)tetrahydropyrazolo[1,5-a]pyrimidine	371.52	372.2
127	3-bromo-5-tert.-butyl-7-(3,4-dimethoxyphenyl)-2-phenyltetrahydropyrazolo[1,5-a]pyrimidine	470.41	470.2/472.1
128	2-[3-cyano-6,7-bis-(4-methoxyphenyl)tetrahydropyrazolo[1,5-a]pyrimidin-5-yl]-cyclopropanecarboxylic acid ethyl ester	472.54	473.0
129	3-cyano-6,7-bis-(4-methoxyphenyl)-tetrahydro-pyrazolo[1,5-a]-pyrimidine-5-carboxylic acid	404.42	405.0
130	4-[3-bromo-6-methyl-2-phenyl-5-(4-trifluoromethylphenyl)tetrahydro-pyrazolo[1,5-a]pyrimidin-7-yl]-phenol	528.37	528.1
131	7-(4-hydroxyphenyl)-6-methyl-2-methylsulfanyl-5-(4-trifluoromethylphenyl)tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	444.47	445.1
132	7-(4-hydroxyphenyl)-6-methyl-5-(4-trifluoromethylphenyl)tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	398.38	399.1
133	2-(4-nitrophenylsulfonyl)-5-phenylsulfanyl-7-pyridin-2-yl-6,7-dihydro-5H-thiazolo[3,2-a]-pyrimidine	510.61	511.2
134	3-(4-chlorophenyl)-5-phenylsulfanyl-7-pyridin-2-yl-6,7-dihydro-5H-thiazolo[3,2-a]-pyrimidine	435.99	436.4
135	5-phenylsulfanyl-7-pyridin-2-yl-3-p-tolyl-6,7-dihydro-5H-thiazolo[3,2-a]pyrimidine	415.58	416.3
136	7-methoxy-4-phenylsulfanyl-2-pyridin-2-yl-3,4-dihydro-2H-9-thia-1,4a-diazafluorene	405.54	406.3
137	7-ethoxy-4-phenylsulfanyl-2-pyridin-2-yl-3,4-dihydro-2H-9-thia-1,4a-diazafluorene	419.56	420.3
138	7-fluoro-4-phenylsulfanyl-2-pyridin-2-yl-3,4-dihydro-2H-9-thia-	393.5	394.2

Exmp.	Name	Calculated Mol. Wt.	Found Mol. Wt.
	1,4a-diazafluorene		
139	3-naphthalin-2-yl-5-phenylsulfanyl-7-pyridin-2-yl-6,7-dihydro-5H-thiazolo[3,2-a]pyrimidine	451.61	452.5
140	7-phenyl-3-phenylazo-5-pyridin-2-yl-3,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-ol	396.47	397.4
141	7-phenylsulfanyl-5-pyridin-2-yl-3,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	380.5	381.4
142	3-phenylazo-7-phenylsulfanyl-5-pyridin-2-yl-3,5,6,7-tetrahydro-pyrazolo[1,5-a]pyrimidin-2-ol	428.51	429.6
143	3-bromo-7-phenylsulfanyl-5-pyridin-2-yl-3,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine	387.3	387.2
144	7-phenylsulfanyl-5-pyridin-2-yl-3,5,6,7-tetrahydropyrazolo[1,5-a]-pyrimidine-3-carbonitrile	333.41	334.2
146	7-(3,4-dimethoxyphenyl)-2-methylsulfanyl-5-pyridin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	407.0	409.5/409.9
147	3-bromo-7-(3,4-dimethoxyphenyl)-2-phenyl-5-pyridin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidine	490.9	492.6/494.4
148	3-bromo-7-(3,4-dimethoxyphenyl)-2-phenyltetrahydro-pyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester	485.9	486.5/488.4
149	3-bromo-7-(3,4-dimethoxyphenyl)-5-(5-nitrofuran-2-yl)-2-phenyl-tetrahydropyrazolo[1,5-a]pyrimidine	524.9	525.4/527.1
150	3-cyano-7-(3,4-dimethoxyphenyl)-2-methylsulfanyltetrahydropyrazolo[1,5-a]pyrimidine-5-carboxylic acid ethyl ester	402.0	402.5
151	3-cyano-7-(3,4-dimethoxyphenyl)-tetrahydropyrazolo-[1,5-a]-pyrimidine-5-carboxylic acid ethyl ester	356.0	357.2
153	7-(3,4-dimethoxyphenyl)-2-methylsulfanyl-5-(5-nitrofuran-2-yl)tetrahydropyrazolo[1,5-a]-pyrimidine-3-carbonitrile	441.5	442.1
154	7-(3,4-dimethoxyphenyl)-5-pyridin-2-yl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester	408.5	409.5

Example 145

3-bromo-7-(3,4-dimethoxyphenyl)-2-phenyl-5-pyridin-2-yl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine dihydrochloride

5 1.5 g of 5-amino-4-bromo-3-phenylpyrazole in acetonitrile were placed in a 100 ml single-necked flask, and 1.55 g of 3,4-dimethoxystyrene, 0.88 g of 2-pyridyl carbaldehyde and 0.72 ml of trifluoroacetic acid were added and the whole was stirred overnight at room temperature. The reaction 10 solution was completely concentrated by evaporation. The crude product was purified by reversed phase HPLC. HPLC column: Macherey-Nagel, VP 100/21 Nucleosil 100-3 C18 HD (serial no. 0115186 batch 23710123) :

15 Gradient: methanol (Riedel-de-Haen, Chromasolv)/water: gradient (4 stages) from 60% to 100% methanol in 37.5 minutes (flow rate 10 ml/min, injection volume: 1 ml) HPLC: Beckman SYSTEM GOLD, (Detector 166, Injector Endurance/SPARK, 125P Solvent Module, fraction collector: Foxy200/ISCO)

20 To form the hydrochloride 139 mg of 3-bromo-7-(3,4-dimethoxyphenyl)-2-phenyl-5-pyridin-2-yl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine were dissolved in 1.1 ml of methyl ethyl ketone and then 6  $\mu$ l of  $\text{H}_2\text{O}$  and 7  $\mu$ l of TMSCl were added. After some time a solid precipitated out. After suction filtration and washing with ether, yellow crystals were obtained that were dried under a vacuum.

30  $^1\text{H-NMR}$  data (600 MHz; DMSO-d6) :

$\delta$  = 8.68 (m, 1H), 8.27 (m, 1H), 7.92 (d, 1H,  $J$  = 8.1 Hz), 7.74-7.67 (m, 3H), 7.39 (dd, 2H,  $J$  = 7.5, 7.5 Hz), 7.33 (t, 1H,  $J$  = 7.2 Hz), 6.83 (d, 1H,  $J$  = 7.7 Hz), 6.78 (s, 1H),

6.66 (d, 1H,  $J = 9.0$  Hz), 5.47 (m, 1H), 5.03 (m, 1H), 3.71 (s, 3H), 3.69 (s, 3H), 2.67 (m, 1H), 2.59 (m, 1H).

Example 147

5 3-bromo-7-(3,4-dimethoxyphenyl)-2-phenyl-5-pyridin-2-yl-tetrahydropyrazolo[1,5-a]pyrimidine, prepared according to the process described above

$^1$ H-NMR data (600 MHz; DMSO-d6) :

10  $\delta = 8.34$  (br. s, 1H), 7.93 (d, 1H,  $J = 3.8$  Hz), 7.64 (s, 1H), 7.14 (d, 1H,  $J = 4.5$  Hz), 6.81 (d, 1H,  $J = 8.3$  Hz), 6.71 (s, 1H) 6.60 (d, 1H,  $J = 8.3$  Hz), 5.40 (dd, 1H  $J = 4.5, 8.3$  Hz), 5.09 (br. d, 1H,  $J = 8.3$  Hz), 3.70 (s, 3H), 3.68 (s, 3H), 2.59 (br. d, 1H,  $J = 13.6$  Hz), 2.50 (m, 1H).

15 Example 152

7-(3,4-dimethoxyphenyl)-5-pyridin-2-yl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile dihydrochloride

20 1 g (9.3 mmoles) of 3-aminopyrazole-4-carbonitrile was placed in 28 ml of acetonitrile, and 2.28 g (13.9 mmoles) of 3,4-dimethoxystyrene, 1.29 g (12 mmoles) of pyridine-2-carbaldehyde and 1.05 g (9.3 mmoles) of trifluoroacetic acid were added and the whole was stirred overnight at room temperature. The dark brown solution was completely 25 concentrated by evaporation in a rotary evaporator and dried. The product was purified by HPLC (conditions as described above).

30 The base that was thereby obtained (270 mg) was suspended in methanol and 15  $\mu$ l of  $H_2O$  and 208  $\mu$ l of TMSCl were then added. A clear solution was formed which was concentrated by evaporation on a Rotavapor. The yellow crystals that were formed were dried under a vacuum.

<sup>1</sup>H-NMR data (600 MHz; DMSO-d6) :

δ = 8.65 (d, 1H, J = 4.8 Hz), 8.23 (t, 1H, J = 7.2 Hz),  
 8.16 (m, 1H), 7.86 (d, 1H), 7.70-7.65 (m, 2H), 6.77 (d, 1H,  
 5 J = 8.3 Hz) 6.68 (s, 1H), 6.53 (d, 1H, J = 8.3 Hz), 5.43  
 (dd, 1H, J = 4.5, 7.5 Hz), 5.08 (m, 1H), 3.70 (s, 3H), 3.68  
 (s, 3H), 2.73 (m, 1H), 2.63 (br. d, 1H, J = 14.3 Hz).

10 Example 56 (dihydrochloride)

The dihydrochloride of 7-(3,4-dimethoxyphenyl)-5-(5-nitrothiophen-2-yl)-tetrahydropyrazolo[1,5-a]pyrimidine-3-carbonitrile was prepared in a similar manner to Examples 145 and 152.

15

<sup>1</sup>H-NMR data (600 MHz; DMSO-d6) :

δ = 8.65 (d, 1H, J = 4.8 Hz), 8.23 (t, 1H, J = 7.2 Hz),  
 8.16 (m, 1H), 7.86 (d, 1H), 7.70-7.65 (m, 2H), 6.77 (d, 1H,  
 J = 8.3 Hz) 6.68 (s, 1H), 6.53 (d, 1H, J = 8.3 Hz), 5.43  
 (dd, 1H, J = 4.5, 7.5 Hz), 5.08 (m, 1H), 3.70 (s, 3H), 3.68  
 (s, 3H), 2.73 (m, 1H), 2.63 (br. d, 1H, J = 14.3 Hz).

Pharmacological investigations:

25 The investigations to determine the NMDA antagonistic action of the compounds according to the invention were carried out on brain membrane homogenates (rat brain homogenate minus cerebellum, pons and medulla oblongata from male Wistar strain rats (Charles River, Sulzfeld, 30 Germany)).

For this, freshly prepared rat brains were digested, after removal of the cerebellum, pons and medulla oblongata, in

50 mmole/l Tris/HCl (pH 7.7) in a Polytron homogeniser (model PT3000, Kinematika AG, Littau, Switzerland) at 6,000 revs. per minute (rpm) for 1 minute while cooling in ice and then centrifuged for 15 minutes at 4°C and 60,000 g.

5 The supernatant was decanted and discarded, and the membrane pellet was taken up again in 50 mmole/l of Tris/HCl (pH 7.7) and digested in a homogeniser at 2,000 rpm for 1 minute and re-centrifuged for 15 minutes at 4°C and 60,000 g. The supernatant was discarded again and the 10 membrane pellet was homogenised in 50 mmole/l Tris/HCl (pH 7.7) (2,000 rpm for 1 minute) and aliquot portions were frozen at -70°C.

15 For the receptor binding test aliquots were in each case thawed out and then centrifuged for 15 minutes at 4°C and 60,000 g. After decanting and discarding the supernatant, the membrane pellet for the binding test was taken up in binding test buffer and homogenised (2,000 rpm for 1 minute). 5 mmole/l Tris/HCl (pH 7.7) supplemented with 20 30 µmole/l of glycine and 100 µmole/l of glutamic acid was used as binding test buffer.

25 1 nmole/l of (<sup>3</sup>H)-(+)-MK801 ((5R,10S)-(+)-5-methyl-10,11-dihydro-5H-dibenzo(a,d)cyclohepten-5,10-imine (NET-972, NEN, Cologne, Germany) was added as radioactively labelled ligand. The proportion of non-specific binding was determined in the presence of 10 µmole/l of non-radioactively labelled (+)-MK801 (RBI/Sigma, Deisenhofen, Germany). In further assays the respective compounds 30 according to the invention were added in concentration series and the displacement of the radioactive ligand from its specific binding to the NMDA receptor was measured.

The batches were incubated in each case for 40 minutes at 25°C and then harvested by filtration to determine the radioactive ligand bound to the brain membrane homogenate.

5 The radioactivity retained by the filter was measured after adding a scintillator ("Ready Protein" scintillator, Beckmann Coulter GmbH, Krefeld, Germany) in a  $\beta$ -counter (Packard TRI-CARB Liquid Scintillation Analyser 2000CA, Packard Instrument, Meriden, CT 06450, USA).

10

The resulting percentage inhibition of the specific binding of the ligand ( $^3\text{H}$ ) - (+) - MK801 in the presence of in each case 10  $\mu\text{mole/l}$  of the respective compound according to the invention serves as a measure of the affinity of this compound for the (+) - MK801 binding site of the ionotropic NMDA receptor. The affinities are given in Table 2 as mean values of double determinations on selected examples.

Table 2

Example	% Inhibition
140	44
141	45
142	75
143	49
144	45

20

The following test conditions were chosen for the determination of the inhibition of the nucleoside transport protein:

25 100  $\mu\text{l}$  of the substance solution in aqueous solution with DMSO as solution aid were incubated for 30 minutes at 25°C

with 100  $\mu$ l of 1.5 nM [ $^3$ H]NB1 ( $N^6$ -benzyladenosine), 100  $\mu$ l of buffer (50 mM Tris.HCl, pH 7.4) and 100  $\mu$ l of an aqueous suspension of erythrocyte membrane. After the incubation the test mixture was filtered off (Whatman GF/C Filter, 5 post-washed with 50 mM Tris.HCl). The filters were transferred to test tubes, 3.5 ml of scintillation fluid were added, and after 2 hours the radioactivity was measured in a  $\beta$ -counter. The measurement results ( $K_i$  value at 10  $\mu$ M and % displacement at 10  $\mu$ M) are shown in Table 3.

10

Table 3

Example No.	$K_i$ Value [ $\mu$ M]	% Displacement at 10 $\mu$ M
39		40
53	0.6	
54	1.3	
55	0.4	
56		43
64	0.6	
111	0.3	
145	0.4	
153		50
154		41

The dihydrochloride of Example 147 (prepared from Example 15 147 in a similar manner to Examples 145 and 152) was investigated as regards its affinity for the recombinant human adenosine A<sub>3</sub> receptor in a displacement assay (C.A. Salvatore et al., *Process. Natl. Acad. Sci. USA* (1993), Vol. 90, 10365-10369). At a ligand concentration of 0.1 nM

[<sup>125</sup>I]AB-MECA (N<sup>6</sup>- (4-amino-3- [<sup>125</sup>I]iodobenzyladenosine) the displacement at a concentration of 3  $\mu$ M was 93%.

5 Pharmaceutical formulation of a medicament according to the  
invention

10 1 g of the hydrochloride of 3-phenylazo-7-phenylsulfanyl-5-pyridin-2-yl-3,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-2-ol was dissolved at room temperature in 1 l of water for injection purposes and then adjusted to isotonic conditions by addition of sodium chloride.

15 The foregoing description and examples have been set forth merely to illustrate the invention and are not intended to be limiting. Since modifications of the described embodiments incorporating the spirit and substance of the invention may occur to persons skilled in the art, the invention should be construed broadly to include all 20 variations within the scope of the appended claims and equivalents thereof.